The New England
Journal of Medicine

VOLUME 215 OCTOBER 8, 1936 NUMBER 15

NEW ENGLAND BRANCH AMERICAN UROLOGICAL ASSOCIATION

NERVOUS DISTURBANCES OF THE VESICAL SPHINCTER*

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Mr. President and Gentlemen:

I THANK you very much for the opportunity to talk to you about the work that I, with the assistance of some colleagues, have been doing in London. I feel some trepidation as a neurologist talking to you about the function of organs of which you all have much more intimate knowledge than I. However, in so far as one might consider micturition as one of those reflexes which are so dear to the hearts of the neurologists, and since the function is largely a reflex one, I will try to justify what I have to say.

I want to speak mainly about the conditions such as one finds in cases where there is a disturbance resulting from a lesion of the cauda equina, for I feel that when these are fully elucidated we shall have a much better understanding of disturbances of micturition resulting from tabes dorsalis and other spinal diseases. As you all know, the bladder and involuntary sphincter have two main sources of innervation. One is derived from the 12th dorsal, 1st lumbar and 2nd lumbar segments, passing through the sympathetic system to the inferior mesenteric ganglion and so down over the brim of the pelvis to reach the vesical plexus as the hypogastric or presacral nerve; the other passes from the 2nd and 3rd sacral nerve roots by way of the cauda equina to the sacral plexus and thence by what is called the pelvic or sacral nerve to the vesical plexus. The disturbance that I am going to talk about is one that brings interruption of the second pathway of nerve supply to the bladder, that is, of the sacral nerve roots which are the origin of the sacral nerve. A lesion of the cauda equina may cause a number of clinical signs, for the sacral nerve roots innervate the muscles of the perineum, the muscles of the calf and the skin segments covering a saddle-shaped area over the perineum, besides bringing to the bladder this second or sacral nerve supply.

*Read before the New England Branch of the American Urological Association, Boston, April 23, 1936.

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It is generally understood that the center for micturition is situated in the sacrolumbar segments of the spinal cord. It is not unusual to find powerful reflex micturition developing in human cases of complete spinal transection above these segments. That is, at intervals as long as six to eight hours there is a powerful evacuation of the bladder, complete, beginning and terminating abruptly. This type of micturition does not immediately follow any sudden damage to the spinal cord. It is preceded by a stage of retention of urine lasting two or more weeks, a state we call spinal shock. Because in some animals, such as the domestic cat, reflex micturition does not emerge from spinal shock after any lesion below particular centres in the brain stem, some authorities postulate a centre for micturition in the brain stem. After transection of the spinal cord in man and in the dog, such fully developed micturition as I have spoken of is of common occurrence and can be demonstrated to depend on distention of the bladder. I believe, therefore, that in man the spinal cord contains, in the lumbosacral segments, all the nervous mechanism necessary for micturition except that which decides whether its occurrence would be appropriate to the environment. Spinal shock has some relation to centres in the brain stem, it is true, but its effect on micturition is the same as its effect on the knee jerk and other spinal reflexes. The state of retention of urine in these circumstances is a state of depression of reflex function.

Happening to observe closely a patient with a cauda equina lesion—a complete destruction of these nerve roots which numbered, in this case, from the lumbar 4th and 5th through all the sacral roots—I noticed that there was not a continuous overflow, as in many such cases, but periodic micturition at long intervals, five or six times a day. There was a periodic complete emptying of the bladder which occurred as a distinct and efficient event, beginning gradually, working up to a steady stream and finishing fairly abruptly, with complete emptying of the bladder. The quantity of discharge was 200 to 300 cc. of urine. The first point one

thought of was that this was not a complete lesion of the nervous system, that in some way this particular man had still some innervation of his bladder from the reflex mechanism in the spinal cord. Every function served by the sacral nerve was completely in abeyance through severe fracture of his lumbosacral spine. There remained, in connection with the bladder, the other source of nerve supply, the hypogastric nerve or presacral nerve which was, with the rest of the lumbar sympathetic outflow, still functioning, as shown by the fact that he could still sweat from his lower extremities (another function of that part of the sympathetic chain) and still perceive pain from the bladder.

Electrical stimulation of the hypogastric nerve causes a contraction of the internal sphincter. If that mechanism were effective in controlling micturition in this particular man, one would have supposed that, in the course of such micturitions as were occurring, he should have been able to stop his micturition by simply contracting his internal sphincter. One was surprised to find that he could not. Once micturition was commenced in any way, either by distending his bladder or by waiting for it to react spontaneously, it went on to its conclusion. He had no power whatever of closing his internal sphincter, though he had still that nerve supply remaining which ought to be able to bring about its closure. Furthermore, by examining the pressure within his bladder by means of a delicate cystometric apparatus, we found that he was quite unable to relax the internal sphincter once it was closed, even though the bladder were quite distended. He had to wait until a micturition occurred spontaneously. The hypogastric or presacral nerve supply to the bladder was of no use to him, either in starting or restraining micturition.

I found that this kind of micturition, "automatic micturition", following destruction of the sacral segments had been observed and described by Müller in 1902[5] and that his observation had been confirmed by others. Müller had further satisfied himself, by excising lengths of spinal cord in animals, that it occurred without any possible mechanism in the sacral segments or in the hypogastric nerve. Elliott[3] found that in animals, and therefore probably also in man, the vesical plexus, the parasympathetic ganglia near the neck of the bladder, contains the essential mechanism. Although establishing the existence of this simple automatic micturition, these investigators were not able to find why in some circumstances it fails to develop, why in many cases of spinal disease there occur permanent states of retention with overflow and what is the sphincteric mechanism which governs its appearance. With a view to gaining information on these points, I, with the assistance of Dr. E. G. Robertson[2] and lately Dr. J. M. Lees, have closely investigated a number of patients with the most complete lesions of the cauda equina or conus medullaris we could find.

The circumstance which decides the onset of micturition in such patients is the reaction of the wall of the bladder to stretching caused by an increasing volume of contents. The bladder began to contract gently as soon as fluid entered it. If the distention ceased for a moment the contraction of the bladder lessened, but was renewed again as soon as distention proceeded further. The more it became distended, the more actively it contracted, so that it reached a point at which the sphincters became patent and micturition occurred. By exerting pressure through the abdominal wall it was possible to raise the pressure of the bladder to twice the value it had reached during micturition without passage of fluid through the sphincter. Passive pressure, within limits, was not capable of forcing the sphincter, whereas half the pressure, provided by a true contraction of the bladder, was sufficient to bring about micturition. Active contraction of the bladder was the requisite for relaxation of the sphincter. With a catheter just distal to the sphincter, the amount of pressure required to overcome the sphincter was found to grow less and less as the bladder filled. When the bladder had only a little fluid in it, high pressure was necessary to overcome the sphincter; as the bladder was stimulated to contract a little by partial filling, less pressure was required to overcome the sphincter; just before micturition was due to occur, only very slight pressure was required to overcome the sphincter. So whatever was the means of obstruction to the outflow of the bladder, it was something which was progressively lessening as the bladder progressively filled. Like micturition itself, it depended on contraction of the bladder, because, if one filled the bladder rapidly and produced a great deal of contraction of its wall, the sphincter became in proportion rapidly very loose. If one filled the bladder suddenly in that way and then stopped filling it so that active contraction of the bladder gradually died away and left only a mild tonic contraction then the sphincter became impassible again, although the volume of fluid in the bladder was just the same. So one might say that the degree of distention of the bladder was not the factor that brought about loosening of the sphincter but rather the amount of contraction that had been induced in the wall of the bladder. Further, it was found that with a fairly rapid degree of distention one could produce waves of contraction in the bladder and with each such wave there was a wave of lessened resistance in the sphincter. So we came

to the conclusion that whatever was the nature of the relationship between the bladder and the sphincter, it was one that was reciprocal with contraction of the bladder. The more the bladder contracted the more the sphincter relaxed; the more the bladder relaxed, the more the sphincter contracted.

These observations were confirmed very soon afterwards on two other cases with complete cauda equina lesions.[2] Later we were fortunate enough to be able to examine a patient who had had the operation of complete presacral neurectomy for megacolon. He had never had any disturbances of micturition and he did not have any after the presacral neurectomy. We found in this patient that, coincident with waves of pressure induced in the bladder produced by distention, there was this reciprocal relationship going on in the sphincter. Therefore, it seems possible to believe that the presacral or hypogastric nerves do not have any more to do with this mechanism than with the process starting or stopping micturition at will. In this fundamental condition of automatic micturition we are dealing with the vesical plexus and its supply to the bladder and the sphincter, and the leading element is contraction of the bladder wall. Without contraction of the bladder wall nothing happens. The sphincter does not work independently. That, of course, is strongly suggested by the very obvious fact that, after a severe spinal lesion, such as transection of the spinal cord or transection of the cauda equina, the first stage is one of complete retention of urine with obstruction at the level of the sphincters. The bladder does not then contract when distended. The capacity of the bladder to contract has to develop first, and only when large enough contractions take place does the sphincter relax sufficiently for micturition to occur.

There are many suggested ways in which the sphincters of the bladder can function. The internal sphincter of Henle is a very insignificant ring-shaped involuntary muscle just at the neck of the bladder. The external sphincter which shields the lower part of the prostate in the male forms a very compact bundle of voluntary muscle, well situated to obstruct the urethra. In normal and in reflex spinal micturition the external sphincter opens and shuts very quickly by means of a reflex mechanism. It is a quickly contracting muscle, whereas the region of the internal sphincter closes and opens in a very gradual way. By cystoscopy the two sphincters can be readily differentiated by the lazy manner of contraction and relaxation of the internal as compared with the sudden snap of the external sphincter. Is the external sphincter responsible for the obstruction in these patients with automatic micturition? One can only say that there is never any sudden snap-like closure. The sphincter always relaxes or contracts slowly and deliberately. This is seen in manometer records just as easily as through the cystoscope. So there is reason to believe that the external sphincter, in common with all the other striated muscles of the perineum in cases with cauda equina lesions, is atrophied and out of function and that its tone is not responsible for what we call the sphincter in such a state.

What then is the sphincter? Young[5] and Wesson[7] proposed, as a result of anatomic observations, that the ring-shaped internal sphincter was opened by a strip of muscle running longitudinally from the trigone and that a contraction of this particular piece of muscle pulled open the internal meatus. The opening of the internal sphincter would in that view be really due to contraction of a muscle which pulled it open, thus making a slit-like appearance of the internal meatus as it was observed by cystoscopy. An important observation in this connection is that originally made by Burns[1] in 1917 and since repeated by many others, namely that in x-rays of the bladder neck, when filled with opaque solution, in many such cases the region of the internal sphincter and the prostatic urethra is found to be dilated into a funnel. The obstruction is distal to what is ordinarily called the internal sphincter. Both in the early stage of partial retention and in the stage of complete automatic micturition this funnel-shaped urethra occurs. Through the cystoscope Burns also observed in these cases dilation of the proximal part of the urethra so that the verumontanum and the walls of the meatus could be clearly seen. Later Schramm[6] also published notes of similar cystoscopic observations. The funnel-shaped urethra in x-ray films and the cystoscopic observation that the most proximal urethra is dilated in a large number of these cases[4] suggest that whatever is the cause of obstruction it is not the internal sphincter of Henle at the bladder neck. Further, the fixity of the prostate in the male and that of the triangular ligament would seem to deny the possibility of any mechanical kinking of the urethra as an explanation of the sphincter mechanism.

With my colleagues, Dr. Robertson and Dr. Lees, I have made a close examination of the phenomenon of the funnel urethra in patients with automatic micturition by making frequent x-ray films of the bladder at various intervals during pressure recording to see how the phenomenon develops and to determine its relation to the contractility of the bladder. When automatic micturition has developed in cases with cauda equina lesions, an x-ray film of the bladder with 25 cc. of opaque solution within it reveals the region of the internal meatus as a small dimple or spike at the base of the bladder. If distention is continued that dimple

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widens and at 100-200 cc. the dimple has opened out to form a small funnel. The urethra is dilating down to the level of the verumontanum. A little further distention causes the funnel to widen until eventually micturition begins; and then a narrow streak is seen to link the tip of the funnel with the bulbous urethra. When micturition is at its height, the urethra entirely relaxes so that the channel is equally wide throughout. There is no question of any mechanical obstruction to the outlet. If the inflow of fluid is stopped at say 100 cc. and the vesical contraction lessens, in the x-ray films the urethra is seen to revert slowly from the funnel to the dimple stage. The fluid in the funnel regurgitates into the bladder, and the urethra closes again. If passive pressure is applied to the bladder suddenly, thus raising the vesical pressure to a high level, an x-ray film during that high peak of pressure shows no reopening of the prostatic urethra; the dimple remains. The funnel cannot be produced by pressure alone. If the bladder is gently massaged, it begins to contract again and after a while the funnel returns. The phenomenon of this widening of the prostatic urethra requires active contraction of the detrusor and is proportional in degree to the contraction of the bladder wall.

That brought us back again to the reciprocal relationship between the active contraction of the detrusor and the sphincter; only we had to consider not the relaxation of a ring-shaped sphincter, but the relaxation of a tube. It was obvious that at low volumes the sphincter could be as tightly shut off in its proximal as in its distal part. Therefore, we were dealing with something which relaxed from above downward. It was as much a sphincter in its upper part as in its lower part. If you filled the bladder suddenly with 200 cc. of radio-opaque fluid and took an x-ray film, you would very likely have found a funnel-shaped dilatation of the urethra, because the bladder was still contracting. Therefore, the obstruction appears to be an active process, not a mechanical one. That brings one to suppose that we are dealing with smooth muscle. This sphincter must be something much more than the small ring-shaped muscle at the bladder neck, the internal sphincter of Henle, because it can contract so strongly all the way down. There is no possibility in its lower part for any mechanical factor. The force that the sphincter can withstand, especially in its lower part, is seen by the fact that the prostatic ducts are often distended by opaque fluid in the x-ray. If that is the case, then we have to consider that the true involuntary sphincter is a tubular muscle which relaxes from above downward by some fixed relationship between it and the detrusor muscle. That relationship appears to be the nervous mechanism of the vesical plexus. My friend Dr. Evans has, with amplifiers, examined the nervous impulses arising from the vesical plexus in animals, and he finds that, when automatic micturition exists, each wave of contraction of the bladder is accompanied by an outburst of nervous discharge from the vesical plexus. Each outburst is distributed both to the detrusor and to the sphincter. One can only suppose that in each wave of activity nerve impulses travel down to the sphincter to relax it, just as those to the detrusor contract that muscle. It is on that elementary neurone of the vesical plexus that all central nervous impulses controlling micturition play. It is the state of depression of that neurone which determines the state of retention of urine that follows sudden damage to the spinal cord or cauda equina.

If the vesical plexus is controlled by the sacral nerves, what does the contraction of the sphincter that can be brought about by stimulation of the presacral nerve mean? There I cannot give you any direct evidence. I think there are two things that are suggestive. In the first place, the contraction produced by direct electrical stimulation of this nerve involves only the proximal part of what we have called the involuntary sphincter. The presacral nerves contract that part of the sphincter which lies just immediately below the bladder neck. Secondly, as we all know, the operation of presacral neurectomy leaves an inefficiency in ejaculation. Further, according to Macalpine,[4] apparently any sort of mechanical lesion or damage to the upper part of the sphincter leaves also a failure of ejaculation without interruption of micturition. It therefore seems reasonable to assume that the contraction of the upper part of the internal sphincter, long observed by physiologists to occur from stimulation of the presacral nerve, is concerned very intimately with the muscular act of ejaculation. It probably has other function as well. In any case we do not necessarily have to bring the presacral nerve into any scheme of the essential nervous mechanism of micturition.

REFERENCES

1. Burns, J. E.: Bladder changes due to lesions of central nervous system. Surg. Gynec. & Obst. **24**:659 (June) 1917.
2. Denny-Brown, D. E., and Robertson, E. G.: On physiology of micturition. Brain **56**:149 (July) 1933.
3. Elliott, T. R.: The innervation of the bladder and urethra. J. Physiol. **35**:367 (July 2) 1907.
4. Macalpine, J. B.: The musculature of the bladder-neck of the male in health and disease. Proc. Roy. Soc. Med. **28**:29, 1935.
5. Müller, L. R.: Klinische und experimentelle Studien über die Innervation der Blase, des Mastdarms und des Genitalapparates. Deutsche Ztschr. f. Nervenh. **21**:86, 1901-02.
6. Schramm, C.: Theoretic and practical considerations in examination by speculum of paretic bladder. Ztschr. f. Urol. **14**:329 (Dec.) 1920.
7. Wesson, M. B.: Anatomical, embryological and physiological studies of trigone and neck of bladder. J. Urol. **4**:279 (June) 1920.
8. Young, H. H., and Macht, D. I.: A contribution to the physiology and pharmacology of the trigonum vesicae. J. Pharmacol. & Exper. Therap. **22**:329 (Dec.) 1924.

DISCUSSION

DR. J. C. WHITE: I think in this country we have been most conversant with the work of Dr. Learmonth which he put out when he was working at the Mayo Clinic. As you look back on this it has led us somewhat astray. The concept that the sympathetic nerves relaxed the bladder musculature and closed the internal sphincter (bladder filling nerves) and that the sacral parasympathetic fibres did the reverse (emptying nerves) was unfortunately a little too simple. The management of a paralyzed bladder would be much easier for us if it were true. As you look back in the literature, and particularly at reports that have come out in *Brain*, you can pick up articles there by Head, Holmes, Fearnsides and Foulds, which contained the right idea back as far as the World War. This work which Dr. Denny-Brown has described tonight is the culmination of it and draws it all together, besides adding a great many new ideas and making it of the greatest value. I think he is to be congratulated on a beautiful piece of physiologic investigation.

DR. GILBERT HORRAX: I think it is quite beyond me to discuss this paper any more than it has been discussed already. I also came, of course, to learn what Dr. Denny-Brown had to say about the mechanism of the bladders concerned with these neurologic lesions. From the point of view of the neurosurgeon, we are interested in whether Dr. Denny-Brown has any clinical applications of this work to the conditions which we see in these neurologic lesions and I wish he might possibly say a word about any such clinical applications which he has. Of course, we are all faced in neurosurgery with spinal lesions or lesions of the cauda equina with this situation of the bladder which we do not perhaps know quite what to do with. There are various ways of handling the situation, some people lean one way and some another. I wonder, in view of what he said of one operation in this paper, whether it would be warranted to try to get along with these cord bladders, especially in traumatic cases and possibly even in some of the tumor cases, not by the ordinary type of manual pressure on the bladder, which at one time was advocated, particularly during the war when we saw so many gunshot wounds, but possibly by a series of manipulations which would start the bladder contractions and thus cause evacuation. I have seen some cases, as no doubt others have seen, of these cord lesions which have done very well with the expression of the bladder manually. On the whole I think, however, that neurosurgeons lean toward the inlying catheter with possibly the method of tidal drainage as advocated by Dr. Donald Munro.

I want to add my congratulations to the others on this piece of work which is certainly interesting and very valuable.

DR. DAVID RIOCH: I was fortunate in having been able to study in Professor Sherrington's laboratory at Oxford in 1929, but unfortunate in that Dr. Denny-Brown had that year completed his work there and had left physiology to go into the field of medicine. I have been particularly interested in Dr. Denny-Brown's paper as it is an excellent example of the thorough and painstaking type of analysis which has characterized the Sherringtonian school from the beginning. Thus, in investigating the nervous control of the bladder his first interest has been to determine the function of the individual efferent nerves and of the intrinsic nervous mechanisms. With these data in hand he has then proceeded to investigate the more complex rôle of the various parts of the central nervous system. This approach is fundamental and much more sure than that used by several other investigators in this field who have started with the central nervous system and then tried to interpret their empirical data.

I am sorry Dr. Denny-Brown did not like the cat, as the cat is an excellent experimental animal. This brings up another interesting point in general about physiology, namely, that we have to study physiology not in one animal and then apply it to all others, but we have to confirm every observation in every species. It has been shown that the sympathetic system is entirely different in its composition of individual types of nerves in the cat, the rabbit and the dog. I believe clinical observations show that the human system differs from those other three forms. In Dr. Denny-Brown's paper we have further evidence of species' differences. In the cat, stimulation of the hypogastric nerves causes the body of the bladder to contract, whereas stimulation of the pelvic nerves causes contraction of the trigonum.

I should like to ask Dr. Denny-Brown whether he has made any observations on the afferent nerves supplying the bladder. In a few experiments we have found that rapidly emptying the distended bladder of chronic spinal cats results in a series of cardiac extrasystoles, so severe as frequently to end in the death of the animal.

I should also like Dr. Denny-Brown to say a few more words about his conception of the mechanism maintaining the contraction of the internal sphincter. Does he assume that the resting state is one of contraction, or is there a nervous center maintaining that tone? Also, does he have any observations upon the hormonal control, such as adrenin in the blood stream acting upon the vesical plexus? This would be of interest since Cannon and Rosenblueth have just shown that the peripheral sympathetic neurons may be sensitized when their preganglionic fibers are cut. It would be of interest also to know whether the different nerves supplying the bladder are cholinergic or adreninergic.

DR. G. G. SMITH: I have seen a number of cases of excision of the rectum which have been followed by marked disturbances of the bladder, sometimes lasting many months or permanently. Of course in that operation the sacral nerves are probably cleaned out along with the rectum and probably the hypogastric plexus also, at least the presacral nerve. I would like to ask Dr. Denny-Brown where the ganglia that control the action of the detrusor are situated. Are they in such a position that they also would be removed or might they be expected in time to give an automatic bladder?

DR. F. H. COLBY: Dr. Denny-Brown has been very nice to come up here from New Haven on very short notice and he has given a splendid paper which we have all enjoyed very much. We are a group that is distinct from his own group and our interest is in practical application of some of these things. I would like to ask him what infection does in instances of cord bladders. Does that modify his previous remarks?

I also am very much interested in what he himself would consider the proper routine in taking care of a patient with a cord bladder. Should these patients be catheterized? Should they be put on constant drainage? Should they be put on tidal drainage? Should they be left entirely alone? Each of these opinions one can find very fervently expressed in urologic literature and it is rather confusing. The internal sphincter apparently isn't of so much account as we have thought. In the operation of total prostatectomy, for instance, we certainly remove the entire internal sphincter and the entire prostatic urethra and I should think the entire vesical plexus,

because the seminal vesicles are removed along with the prostate, yet a certain number of these individuals have normal micturition after the operation. I mean they are not incontinent.

DR. J. D. BARNEY: I am wholly unable to discuss Dr. Denny-Brown's masterly exposition on the subject, but I would like to ask a question. Some years ago I was very much interested in the subject of tabetic cord bladders and carried out a lot of clinical observations. We had patients with tabes who were totally unable to urinate perhaps more than a few drops; some had complete retention and some had almost complete retention. After proper training, so-called Fraenkel exercises, we were able to re-educate these bladders so that they had good function and to a point where they had no residual urine at all. This went on in many cases perfectly indefinitely. We do not seem to hear so much about this method as we used to, but I remember it was done with great success a good many years ago. I suppose there was damage to the nerves of the bladder supply but not to the muscle. After being wholly out of action for a long time, they resumed function perfectly well. Perhaps Dr. Denny-Brown can explain why that happened.

DR. E. GRANVILLE CRABTREE: I haven't anything to add except that I have been enjoying myself listening to what sound like very sound ideas.

DR. DENNY-BROWN: I am very grateful for the way you have received my contribution and to all who have made such appreciative remarks. Of course there are still dozens of questions which involve this very complicated subject.

First of all, the external sphincter. Certainly in normal man, and in cases of reflex micturition, by which I mean cases of transection of the spinal cord with reflex activity of the spinal segments below the lesion, the external sphincter is closed except during micturition. The activity of the detrusor appears to be the only thing that effects its opening. In a normal man, with the bladder moderately distended, the external sphincter cannot be induced to open unless the bladder contracts. This sphincter is constantly shut and is relaxed by means of a reflex through the lumbosacral segments. It reinforces the involuntary sphincter.

The funnel type of relaxation of the involuntary sphincter occurs in normal man, as in cauda equina lesions, but occurs very much more rapidly, so that in the course of ordinary micturition, the whole cycle represents the opposite of the sudden contraction of the detrusor. It is just as rapid after spinal transection. There is, therefore, a big difference between the lesion that leaves the spinal cord active and one that destroys the sacral nerves. You might say that in spinal transection, the bladder appears to wait up to a point and then contracts suddenly. Furthermore, it is true that this funnel phenomenon of Burns is more commonly encountered in states such as syphilis of the spinal cord and other nervous diseases associated with retention of urine and dribbling, particularly where there is loss of tendon jerks and some loss of function of the dorsal columns of the spinal cord. In these states there is a persistent partial relaxation of the urethra corresponding to persistent partial contraction of the bladder, half way between these other two. I have chosen to talk about the cauda equina lesion because there is a simple transection of one particular nerve supply, whereas in tabes there is a more complicated state of affairs. The dorsal nerve roots are damaged and the dorsal columns are damaged, and there is no sure way of estimating just how much the disturbance of function is due to each. As a result of examination of a large number of neurologic conditions, the one factor that does cause a persistent state, midway between automatic and reflex micturition, is damage of the dorsal columns of the spinal cord. With all such cases we find this funneling. In all of them, stages of mild, persistent retention are associated with mild, persistent vesical contraction.

Of the manner in which infection affects this process, automatic or reflex micturition can develop from states of retention in the presence of the most gross infection. In other cases, in the absence of any gross infection, it sometimes fails to develop efficiently. Just why sometimes the mechanism survives and sometimes lapses does not appear to depend on the degree of infection of the bladder, though certainly it is affected by any pyemia. The bladder then reverts to its original state of retention of urine with continued contraction of the internal sphincter.

Dr. Rioch has asked what makes the internal sphincter contract. I can only answer in terms of the anal sphincter, because the vesical sphincter is very difficult to observe directly. We found that in man, the rectum and the anus behaved in exactly the same way as the internal sphincter of the bladder. The internal anal sphincter is undergoing just the sort of change in just the same conditions as the bladder but it can be examined much more easily. There it is quite obvious that, if the rectum is not contracting, the internal anal sphincter is firmly closed. If an apparatus is devised to distend it degree by degree from nothing up to a wide distention, it is found that its contraction is in proportion to the amount of distention. If nothing is distending the sphincter, it does not contract. Apparently such a mechanism would explain what the vesical sphincter does. It does not maintain unmeaning contraction, but it has what really is an essential feature of all tonic contraction, that is, a reaction to stretch. Once it is stretched by any fluid tending to pass it, it contracts. Whether this reaction is determined by a nervous plexus or is a purely muscular phenomenon remains to be determined by physiologists. An interesting point is that it seems to be the particular function of all sphincters to preserve a reaction to stretch and only active contraction of the canal above can affect them.

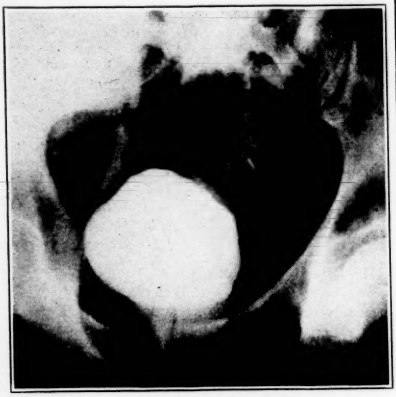
Dr. Rioch also asked about chemical or hormone control, such as by adrenin or acetylcholin. I am afraid I am unable to tell him anything about that except that the nervous origin of this process is suggested by the fact that not only does the automatic bladder react with discrete micturitions, but, if you give sudden pressure on the bladder, it contracts with an immediate extra wave of contraction. The whole process appears to be too rapid for chemical stimulation. It appears to be a direct nervous reaction to stretch.

Dr. Horrax has asked me about treatment and I am afraid, like everybody else, I see cases do well under various treatments, by continuous catheterization, by catheterization at intervals, by tidal drainage and so forth. Some of these conditions seem to recover more quickly than others, but just why does not seem to depend so often as it should on the way they are treated. One finds contradictions right and left. Again I feel that we really do not know enough about the principles underlying the vesical mechanism. I am quite aware that valuable work is being done, particularly in this country, on cystometry, but still I feel that we have a great deal more to learn about the mechanism. I think the information gradually accumulating from systematic tidal drainage and other means of following cases through from beginning to end will eventually give us much better insight into the many problems which should be settled. Until then there cannot be said to be any rational basis for this or that treatment. I think gentle massage of the bladder in such diseases as tabes is a sound procedure in encouraging the bladder to contract and in securing more efficient micturition.

A CASE OF "AUTO-PROSTATECTOMY" DUE TO TUBERCULOSIS*

BY THOMAS N. HEPBURN, M.D.†

I AM taking the liberty of presenting this case of complete destruction of the prostate by tuberculosis and its extrusion through the urethra under the name of "auto-prostatectomy", so as to put this pathologic phenomenon in correlation with what we have long called "auto-nephrectomy" by tuberculosis.



Cysto-urethrogram showing "auto-prostatectomy" by tuberculosis.

Eight years ago I removed a tuberculous left kidney and ureter from this twenty-six year old man. At that time there was no evidence of genital infection. He was not conscious of any disability in these regions until two years ago when he returned to me and I made a diagnosis of prostatic tuberculosis. I advised general hygienic treatment. Two months ago he reported again feeling quite well, but complaining of dribbling following urination. The cysto-urethrogram shows the picture here presented in which the prostatic tissue has been entirely extruded through numerous dilated ducts in the floor of the urethra, and its place is taken by a diverticulum bounded by the prostatic capsule and opening into the prostatic urethra.

Although both the external and the internal sphincters are normal, the posturinary dribbling from this prostatic cavity which is filled with urine at each urination is easily understood. As soon as this cavity has emptied, his continence is perfect.

On cystoscopic examination, this man's bladder is normal. The floor of the prostatic urethra is perforated with numerous dilated prostatic ducts varying from 1 to 5 millimeters in diameter. The verumontanum and ejaculatory ducts appear perfectly normal.

Rectal examination shows no suggestion of tuberculosis of the seminal vesicles, and there is no evidence of epididymitis.

We have here a case of tuberculous prostatitis in which the infection was carried by the urine through the prostatic ducts into the prostate with no apparent evidence of involvement of the seminal vesicles and epididymes. Furthermore, we have a pathologic process by which nature has quite successfully taken care of its own destructive products without injury to any surrounding tissues. In my own experience I have never seen this before and a casual search of the literature on genital tuberculosis has failed to reveal a report of this very happy, natural method of "autoprostatectomy".

*Read before the New England Branch of the American Urological Association, Boston, April 23, 1936.

†Hepburn, Thomas N.—Urological Surgeon, Hartford Hospital. For record and address of author see "This Week's Issue," page 683.

URETERO-URETERAL ANASTOMOSIS*

With Report of a Case

BY C. H. NEUSWANGER, M.D.†

WHILE experimenting with various methods of transplanting the ureter in our laboratory in New Haven, a simple technic was evolved.

This consists simply in cutting the ureter obliquely and placing a black silk stitch in the tip of the ureter; both strands are then threaded through a large straight needle and the transplantation is effected by passing the needle through the recipient tissue. This is followed in turn by the ligature and ureter. This procedure is best illustrated by figure 1. This illustration represents uretero-ureteral anastomosis carried out in dogs.

This method was found admirably adapted

*This research work was made possible by a grant from the Research Funds of the Yale University School of Medicine.
Read before the New England Branch of the American Urological Association, Boston, April 23, 1936.

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for repairing a cut ureter and for uretero-ureteral anastomosis.

Following the use of this method on thirty-two animals over a period of four years with good results, it was used on a clinical case which I shall report.

Uretero-ureteral anastomosis has been considered in the past as surgical gymnastic and dismissed chiefly because of the danger of stricture formation. To my knowledge the case here presented is the second one reported on man, the other being an end-to-side anastomosis.

CASE: J. K., a male, thirty-six years old, had complained of blood in the urine for three and one-half years. The patient was seen by a doctor in February, 1935, who fulgurated three papillomas about the left ureteral opening. March 7, 1935, he was examined at the New Haven Hospital and found to have three papillomas, one emerging from the left ureteral opening, one to the left of the opening and one on the left of the ureteral ridge. Biopsy was done and the tissues fulgurated. Fulguration was repeated on March 28, 1935; and, on July 25, 1935, all three tumors had recurred and fulguration was again done. On August 9, 1935, fulguration was done under an anesthetic and the tumor in the ureteral orifice was fulgurated deeply. Following this, a course of x-ray treatment was given. On December 11 a complete cystoscopy showed both kidneys to be normal, but there was a recurrence of the tumors with extension into the lower 2 centimeters of the left ureter.

Operation was done on December 18, 1935, at which time the left ureter was transplanted into the right by the same method as described above. The stump of the left ureter together with a portion of the bladder bearing the tumors was removed. Convalescence was uneventful. There was no leakage of urine at any time. Three months later intravenous urography showed the kidneys and ureter to be unchanged and an anastomosis functioning normally.

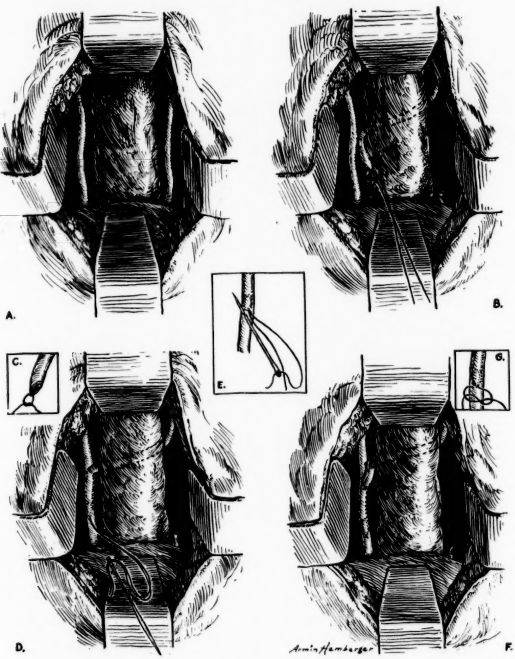


FIGURE 1.

CONCLUSIONS

This method of transplantation avoids to a large extent the danger of peritonitis and subsequent infection of the kidneys. In selected cases where there is need of transplantation of one ureter this method may prove of value if our clinical results prove as satisfactory as those obtained in animals.

DISCUSSION

DR. G. G. SMITH: When you put the ureter from the diseased side into the other, are you not afraid it will occlude the lumen of the healthy ureter and in that way possibly destroy the function of the kidney? How do you explain the avoidance of that?

DR. CLYDE DEMING: I think Dr. Neuswanger has given you most of the details but Dr. Colby has asked if it could be done through the peritoneal cavity. It has been done retrovesically and extraperitoneally so that the peritoneum is not opened at all.

In regard to obstruction at the point of anastomosis, it seems clear that we do not get an obstruction. The one and only experimental case of that, as far as the dogs were concerned, was the one which Dr. Neuswanger presented to you. Whether we have the correct interpretation in regard to that case I don't know, but it is interesting to note that one can do this safely and without apparently any obstruction at the point of anastomosis. We hesitated to present it to a larger body but we would like to have you talk it over and make any suggestions or criticisms you would like about such a procedure. Perhaps the physiologists could explain the reason why you don't get an obstruction at that point. Certainly in all the experimental work, there has been no definite obstruction at the point of anastomosis.

DR. NEUSWANGER: Dr. Smith's point is well taken. At the first operation in which we transplanted one ureter into the other I thought we would surely get a hydronephrosis but the ureter simply dilates, the extra lumen which is in the second ureter causes a little local dilatation and it apparently doesn't take much room for the urine to get by. I have one animal which Dr. Deming has made me keep. This is her third year but I expect to autopsy her some of these days and I don't believe she will show any hydronephrosis. Unfortunately, it is difficult to get an x-ray of these animals without killing them. You cannot possibly catheterize these ureters and if you inject intravenous skiodan you don't get satisfactory pictures.

THE IMMEDIATE EFFECT OF PREOPERATIVE RADIATION IN CORTICAL TUMORS OF THE KIDNEY*

BY GEORGE C. PRATHER, M.D.,† AND HARRY F. FRIEDMAN, M.D.†

STATISTICS from various clinics indicate that the outlook for patients with malignant tumors of the renal cortex has not been a pleasant one. There has been a high operative mortality with only a small percentage of five-year cures in the group which has survived nephrectomy.

Hyman[1] reported a group of 5 to 10 per cent that were not operated on because of the extent of the tumor or because of metastases. Judd and Hand,[2] reporting in 1929, showed that only 10 per cent of their patients with renal tumor had survived nephrectomy for ten years. Smith[3] found of those who survived operation that 47 per cent of those with hypernephromas and 77 per cent of those with adenocarcinomas died of a recurrence. He reported a 25 per cent survival of his cases without evidence of recurrence for a period varying from one to ten years. Smith and Shoemaker[4] in a previous report found of those who had nephrectomy that nearly 50 per cent were dead within one year. In children the outlook appears to be even worse. Statistics collected by Wharton[5] indicate that 90 per cent of the children with renal tumors have died within one year after operation.

Operative mortality is influenced to some extent by the enthusiasm of the surgeon as well as by his skill. There has been a group of large tumors on which most men would refuse to operate. Others would make the attempt, obtain a microscopic diagnosis and back out, while the more daring soul would proceed to remove the tumor with an immediate mortality. In a series of nineteen cases which Smith and Shoemaker explored but in which they could not do nephrectomy, only two patients lived more than a year. Thus the operative mortality can be high or low without significance, except for the pertinent fact that, in the group which have had nephrectomy in the past, there has been an operative mortality of 15 to 30 per cent. In his own series of forty cases Smith found an operative mortality of 17.5 per cent. Wharton has found that the reports of Swan, Hunt and Wollstein indicate that between 12 and 26 per cent have had only exploratory operations, due to the extensive pathology present.

To summarize briefly, the literature demonstrates that about 5 per cent of these tumors are too extensive when first seen to warrant surgical consideration. Another 12 to 26 per cent have been explored and found inoperable. Of those who have been nephrectomized 15 to 30 per cent die as the result of operation. Therefore, between 35 and 60 per cent of all patients who have been seen with renal tumor have never reached a place in any program of therapy which would give them a chance of a materially extended survival.

Even though Mintz[6] reported four cases which survived an average of eight years after diagnosis before nephrectomy or autopsy was done, the average natural history of these tumors probably covers a much shorter period of time. Walker[7] reports E. Garceau as stating that in thirty-two cases the average interval between the first symptom and the fatal issue was three and one-half years. In twenty-eight cases reported by Smith and Shoemaker in which the kidney was not removed the average duration

*Read before the New England Branch of the American Urological Association, Boston, April 23, 1936.

†Prather, George C.—Assistant Urologist, Beth Israel Hospital and Boston Lying-in Hospital. Friedman, Harry F.—Attending Radiologist and Director of Tumor Clinic, Beth Israel Hospital. For records and addresses of authors see "This Week's Issue," page 683.

of life after the first symptom was less than two years in twenty-five cases.

The important factor, that contributes to these failures, exclusive of the potent fact that we are dealing with cancer, is the size of the tumor. It balks our surgical efforts—first, by prohibiting surgery in some, secondly, by discouraging nephrectomy in others and thirdly, by proving surgery insufficient to cure in many instances when nephrectomy has been accomplished.

It has, therefore, been of the greatest interest to hear of the encouraging reports of Waters,[8] Bothe,[9] and Wharton,[5] in the use of the Coutard type of preoperative irradiation to reduce the size of these tumors. Their clinical and histologic studies show that many tumors of the renal cortex will diminish in size in a spectacular manner. This has held true apparently in tumors composed of embryonal, poorly differentiated cells which lack a tough membrane. Bothe reports reduction in size of 40 to 50 per cent in two mixed tumors of the kidney which he irradiated. The series of fifteen cases reported by Waters, Lewis and Frontz[10] has shown 93 per cent radiosensitivity. Wharton reports two Grawitz hypernephromas and two Wilms' embryomas which decreased in size almost miraculously. To this group I can add one Wilms' tumor and two hypernephromas which were definitely reduced in size by preoperative irradiation (cases 1, 2 and 3). A fourth case, carcinoma simplex of the adrenal (case 4), did not appear to be influenced. In the small number of cases reported to date, therefore, we have reason to be pleased with this method of temporarily reducing the size of cortical tumors of the kidney.

Microscopic examination of the specimens which have been irradiated shows necrosis as a constant finding. Necrosis, however, is found in many large nonirradiated tumors. Some fibrosis is evident. Waters reports thickening of the capsule which we are unable to observe, while Bothe mentions in the Wilms' type of tumor which he studied that irradiation had a definitely destructive effect upon the embryonal connective tissue cells, but little or no effect upon the better differentiated epithelial cells.

After careful microscopic study of the four cases reported here we agree that, while irradiation seems to produce definite gross and microscopic changes in these tumors, it does not cause a cure. Bothe reported three children who so improved under irradiation treatment that their parents would not permit surgery. Two of the three were dead within a year.

The technic used in these cases has necessarily varied on account of the different types of tumors and the extent of the tumors as revealed by palpation and pyelogram. We have attempted in all cases to give what we considered the maximum amount of irradiation that these patients would stand, realizing that the lethal roentgen dose for hypernephroma is probably prohibitive. In the case of the Wilms' tumor (case 1) we felt that we might be able to destroy it by the dosage given, and, as judged from the postoperative histologic evidence, we came very near attaining our purpose. The technic used in this case consisted of the following factors: 200 K. V. pulsating, 4 milliamperes of tube current, .75 millimeter copper and 1 millimeter aluminum filter, 50 centimeters tube distance, wave length effective 0.16 A units, quantity 10.5 roentgens per minute, field 150 square centimeters, 4000 roentgens total dose, 200 roentgens daily dose for 20 days, alternating front and back over the mass. This dose was repeated to the kidney bed following operation. The amount of radiation given in this case is, we feel, the low limit for a Wilms' tumor and should be increased in those cases that can tolerate it. This little patient was too poor an irradiation risk to attempt a larger dose, although the response was most gratifying. The tumor could not be made out on palpation and appeared only as a walnut-sized mass in the pyelogram.

Case 3 presented a huge mass in the right side of the abdomen and the typical roentgen findings of a cortical tumor. The lethal dose for a hypernephroma, in so far as we are aware, has never been determined. We have given as high as 9000 roentgens directly into the mass through three fields of 180 square centimeters, anterior, posterior and lateral. This has produced a destruction of the germinal layer of the skin with denudation of the dermis. In the microscopic examination of this tumor one was able to distinguish live tumor cells. There was considerable fibrosis and a great deal of necrosis. No intestinal symptoms were noted in any of our cases. The blood remained unchanged and the skin returned to its normal texture in two weeks. Two weeks following the irradiation, the tumor had decreased to half its size to be followed by an increase for a period of ten days. We wish to call particular attention to this phenomenon which apparently is due to edema caused by the irradiation. The mass just before operation was about one-third of its original size. In the treatment of this case the following factors were used: 200 K. V. pulsating, 4 milliamperes of tube current, 2 millimeter copper and 1 millimeter aluminum filter, 50 centimeters tube distance, wave length effective 0.12 A units, quantity 3.5 roentgens per minute, 3 fields of 180 square centimeters anterior, posterior and lateral, 3000 roentgens to each field, daily dose 200 roentgens to each of two fields morning and afternoon, total dose 9000 roentgens.

Case 2 was treated in the same manner as the case above, the total dose being 6000 roent-

gens. The posterior field was increased to 400 square centimeters which necessitated decreasing the amount of irradiation to this field.

Two of our four patients remained in the hospital the first week of their treatment and then called daily for their treatment. The other two were ambulatory patients from the beginning of treatment. All four patients had some nausea and vomiting during the course of their treatment but this was not sufficient for them to be called miserable. They did not lose weight. The white blood count did not go below 6000. None of them were transfused during the course of irradiation or before surgery. They all gained appreciably in general health between the conclusion of irradiation and date of nephrectomy, a period which varied between ten and thirty days. A definite tanning of the skin took place in the three renal cases. In none of these four patients was there any delay in healing of the nephrectomy wound. They all had a normal convalescence. There was no noticeable perirenal fibrosis or difficulty with adhesions at the time of operation.

By frequent observation of these patients during their irradiation treatment we have gained the impression that decrease in size of the tumor began about the third week of treatment and that the tumor had not started to enlarge again at the time of operation. Furthermore, the general condition of the patient began to show rapid improvement two to three weeks after the conclusion of irradiation treatment. We believe, therefore, that an interval of at least three to four weeks between the conclusion of irradiation and nephrectomy is probably desirable.

Just what the optimum dose of irradiation is for this type of tumor and what the optimum interval should be between the conclusion of the irradiation program and the nephrectomy, has not been finally determined.

The immediate effect of preoperative radiation will be of value if it will reduce the size of the tumor to permit a safer and easier nephrectomy.

CASE REPORTS

CASE 1. F. G. Male—aged 3½ years. The patient seen July 10, 1934.

Two weeks previously his mother had noticed a lump in the right flank. A doctor was called and advised immediate surgical consultation. A general surgeon operated that night, found a solid retroperitoneal tumor and obtained a biopsy. Biopsy report—Wilms' tumor. Further surgical consultation offered the family no hope.

P. E. Slender boy, pale. Abdomen showed a mass in the right flank extending past the midline anteriorly from the false pelvis to the diaphragm. The abdominal incision had healed. One stitch was still in place. The urine was negative.

Diagnosis: Wilms' tumor of the right kidney.

Radiation was given by Dr. Friedman between July 11 and August 6, 1934, inclusive, consisting of 20 high voltage x-ray treatments in doses of 200 'r,' for a total of 4000 'r' units.

An intravenous pyelogram was made August 26, 1934 (fig. 1).

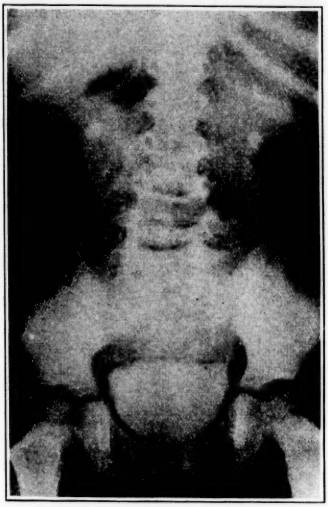


FIG. 1.

F. G. Case 1. Right Wilms tumor. Intravenous pyelogram still showing some distortion of right kidney following 4000 'r' units preoperative radiation. There has been a remarkable reduction in size due to radiation.

An extraperitoneal nephrectomy was done August 29, 1934. The tumor had receded to where it was barely palpable on physical examination (fig. 2).

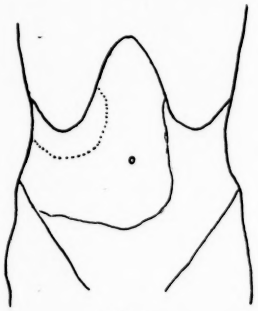


FIG. 2.

F. G. Case 1.
Solid line—preradiation estimate as to size of tumor.
Dotted line—postradiation estimate as to size of tumor.

Nephrectomy was accomplished easily except on the peritoneal surface through which the biopsy incision had been done. The convalescence was uneventful.

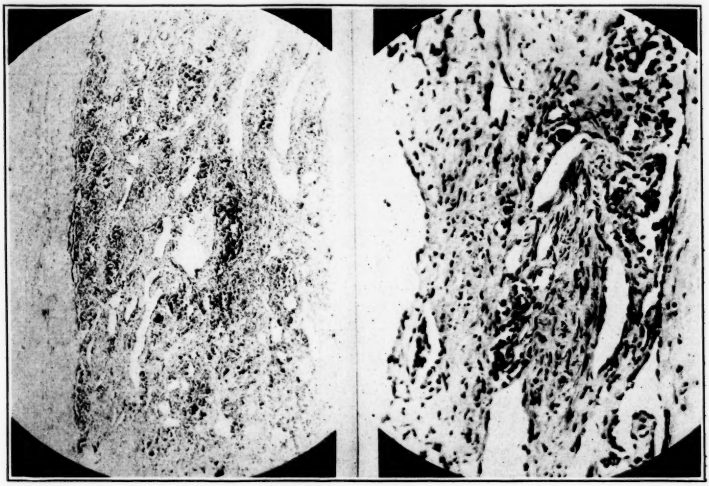


FIG. 3.

F. G. Case 1. Wilms tumor following 4000 'r' units radiation. The original tissue of the tumor is destroyed and fibrosed and there are only occasional islands of cells which look like epithelial cells. Enclosed by a thick fibrous capsule is a very vascular fibrous tissue tumor. There is no inflammatory reaction.

The pathologic report on the kidney finally removed was "Fibrosed tumor of the kidney (fig. 3). possibly Wilms' tumor."

In October, 1934, the patient had 4000 'r' units as a postoperative measure, making daily visits to the office of Dr. Friedman. It is now nearly two years since the operation and there is no evidence of recurrence or metastasis.

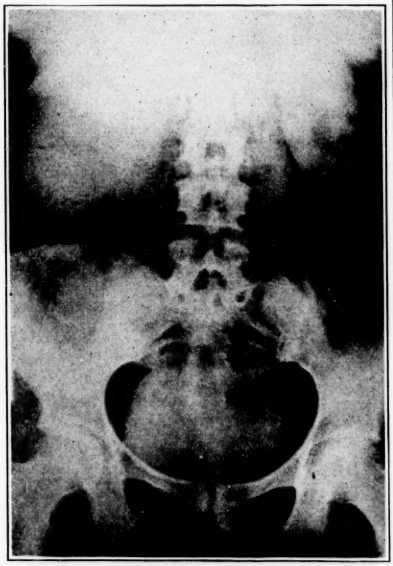


FIG. 4.

Case 2. Right hypernephroma. Right pyelogram before radiation. Distortion of calices poorly shown in the print.

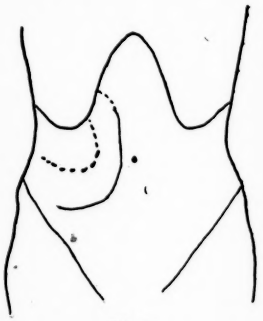


FIG. 5.

R. C. Case 2.
Solid line—preradiation estimate as to size of tumor.
Dotted line—postradiation estimate as to size of tumor.

CASE 2. R. C. Female—aged 50 years. On September 8, 1935, the patient developed gross hematuria. The following day she had sudden, acute pain in the right costovertebral region, radiating to the right lower quadrant.

P. E. Her blood pressure was 160/100. A tumor in the right upper quadrant the size of a grapefruit was found which was slightly tender. The

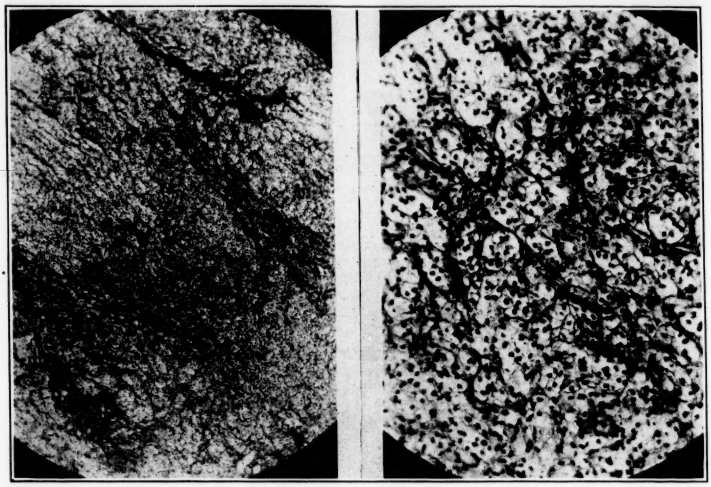
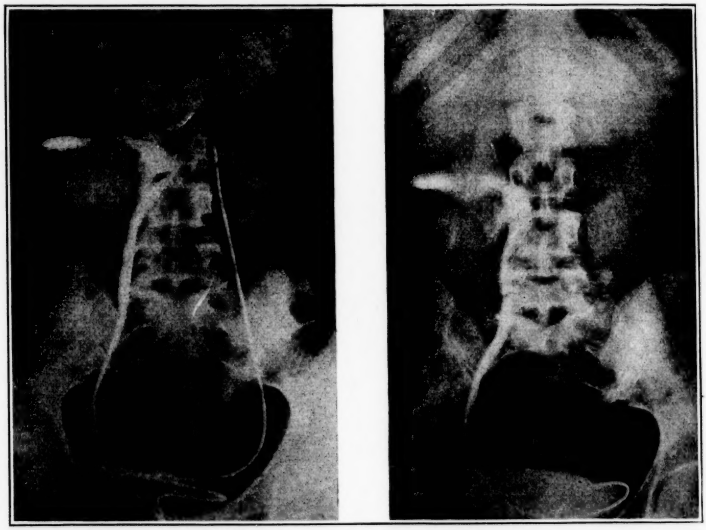


FIG. 6.

R. C. Case 2. Hypernephroma following 6000 'r' units radiation. There are large cells with cytoplasm peculiarly clear so that it has a foamy appearance. Cells are arranged in cords for the most part. There is a loose connective tissue. Glomeruli and tubules appear in good condition. Very little histologic effect from radiation.



A B

FIG. 7.

A. F. Case 3. Right hypernephroma.

A. Right pyelogram before beginning radiation.

B. Right pyelogram three weeks following 9000 'r' units preoperative radiation.

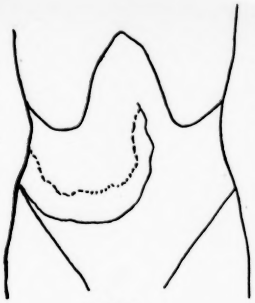


FIG. 8.

A. F. Case 3.
Solid line—preradiation estimate as to size of tumor.
Dotted line—postradiation estimate as to size of tumor.

FIG. 9.

A. F. Case 3. Gross specimen of hypernephroma of the right kidney after 9000 'r' units radiation.

mass was irregular and moved very little with respiration.

Laboratory notes: Urine—s. t. albumin, no sugar, sediment loaded with red blood cells with occasional white blood cells. Blood, nonprotein nitrogen, 39; Wassermann negative.

An intravenous pyelogram was done September 11 and showed a right hypernephroma (fig. 4).

X-ray treatment was started. Daily treatments and hospitalization during the next fourteen days, following which time she continued having x-ray treatments at the office of Dr. Friedman. Radiation was finished October 1. The patient had 6000 'r' units through three portals.

Transperitoneal nephrectomy was done October 10, 1935, by Dr. E. G. Crabtree who thought the tumor was smaller than previous to x-ray (fig. 5). The postoperative convalescence was uneventful.

Pathologic report was "hypernephroma" (fig. 6).

A follow-up four months later showed no evidence of recurrence.

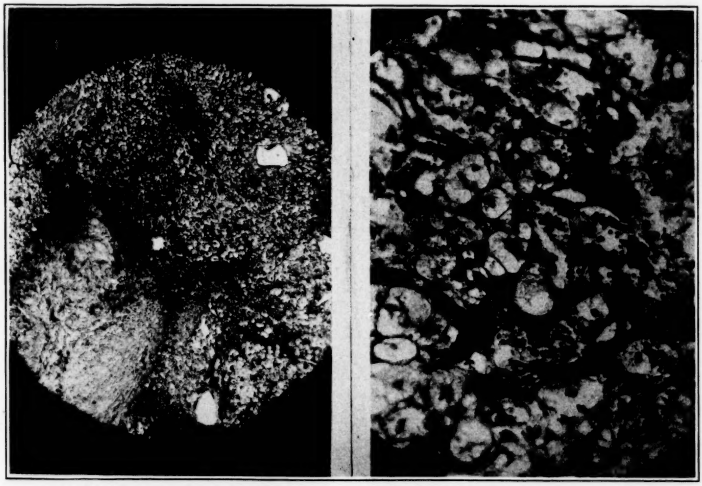


FIG. 10.

A. F. Case 3. The tumor was mostly on upper pole.
Slides—only a slight suggestion of normal kidney tissue seen. Through all sections is a marked scattering of atypical cells. Cells are large with a fairly definite cellular membrane. These cells tend to form cord-like masses. In many areas there has been marked degeneration within this tumor tissue and much hemorrhage is noted. Hypernephroma of kidney (with necrosis).

CASE 3. A. F. Female—aged 52 years. The patient complained of hematuria with right colicky pain, radiating from right back to epigastrium, of one week's duration.

She had had kidney trouble as a child while in Russia and was "swollen all over" and was in the hospital three weeks.

P. E. A large mass was found in the right upper quadrant, the right flank and the epigastrium.

A pyelogram demonstrated a hypernephroma (fig. 7).

FIG. 11.

F. R. Case 4. Right pyelogram of adrenal tumor with some distortion upper calyx of kidney. Kidney pushed downward slightly. Increased density above the kidney with diffuse calcification in the adrenal tumor.

X-ray treatment was begun December 12, 1935 and was concluded January 13, 1936—a total of 9000 'r' units being given.

On January 14, 1936, there was some erythema with vesiculation and the patient remained one week in the hospital for vaseline dressings.

On January 30, 1936 the skin was in good condition.

On February 8, 1936, a definite reduction in size of the mass was found (fig. 8).

On February 12, 1936, transperitoneal nephrectomy was done without difficulty, ligating the pedicle before isolating the tumor (fig. 9).

The pathological report was "hypernephroma" (fig. 10).

The convalescence was normal.

Two months later there was a definite gain in weight and strength with no evidence of recurrence or metastases reported.

CASE 4. F. R. Female—aged 20 years. This patient was a twenty year old girl who had had amenorrhea for seven years. At the same time she had developed hypertrichosis and her voice had become definitely masculine in character. The late Dr. Delbert Jackson had explored her pelvis six years ago and had found polycystic ovaries with thickened, tough capsules. Various ovarian extracts had been tried without effect. Two years ago there was a slight rise in blood pressure, ranging between 140 and 150 systolic. This raised the question of adrenal hyperplasia.

The patient was first seen by Dr. Prather for Dr. Charles Lawrence in the summer of 1934. Intravenous pyelography was done. There was nothing to be felt in the abdomen. The urine was negative and the physical examination disclosed the changes previously described. There were no changes in the labia or clitoris. Pyelograms indicated a mass above the right kidney. Adrenal tumor was suspected but with symptoms of such long standing it seemed wise to wait and repeat the pyelographic study.

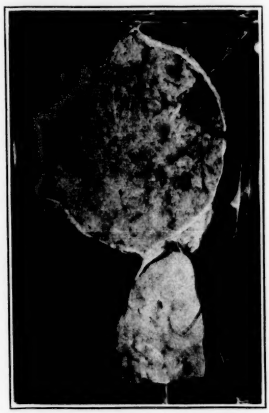


FIG. 12.

F. R. Case 4. Adrenal tumor with upper pole of right kidney. No change in size following 3000 'r' units of radiation.

The pyelogram was made in March, 1935, and showed the same x-ray findings as on previous intravenous pyelography (fig. 11). It seemed probable that this patient did have an adrenal tumor, the type of which was unknown. She, therefore, finished her school year and had 3000 'r' units of preoperative radiation at Dr. Sidney Morrison's office. At no time was there any palpable mass in the abdomen or right costal region.

The pyelograms were repeated immediately before operation and showed no change in the size or appearance of the suprarenal mass. A chest plate was negative. Three weeks after completing her preoperative radiation, surgery was done on July 25, 1935, finding an encapsulated adrenal tumor attached to the upper pole of the right kidney. Both organs were removed (fig. 12). The pathological report was "carcinoma simplex of the adrenal. Normal kidney" (fig. 13).

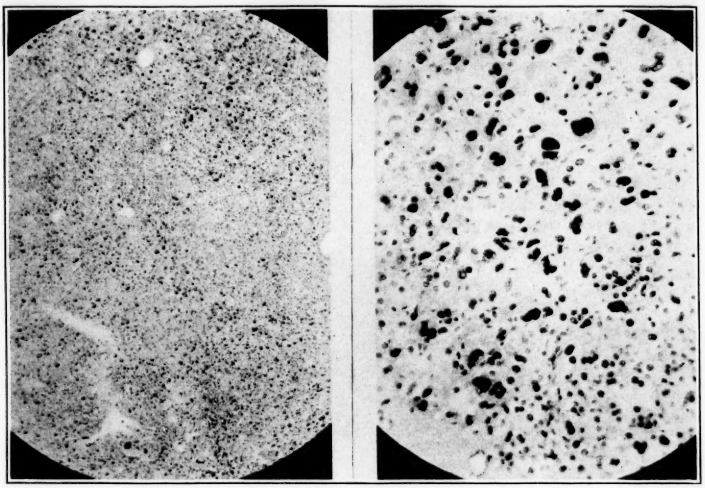


FIG. 13.

P. R. Case 4. Adrenal tumor following 3000 'r' units radiation. Carcinoma simplex of adrenal. Tumor mass shows capsule composed of fibrous tissue in which are present streaks of columns of cells with round nuclei and pale cytoplasm, resembling adrenal cortical cells. Some of the nuclei are of huge dimension, many cells have many nuclei. The cytoplasm is abundant and of a pale eosin-staining type. The stroma is slight, composed in general of many capillaries, separating single and groups of tumor cells.

The convalescence was uneventful. Adrenal cortex hormone was on hand and was used routinely for three days by Dr. Lawrence.

The patient was discharged three weeks after operation.

Her periods reappeared in September, 1935 after an absence of catamenia of seven years' duration.

Her family and Dr. Charles Lawrence believe the pitch of her voice has become raised. There is no change in the rate of growth of facial or abdominal hair.

SUMMARY

1. About 5 per cent of renal cortex tumors have been too extensive when first seen to warrant surgery.

2. Twelve to 26 per cent have been explored and found inoperable.

3. Nephrectomy has shown a mortality rate between 15 and 30 per cent.

4. With exceptions, the average natural life history of these tumors is two to three and one half years.

5. Reports indicate that preoperative radiation will reduce the size of these tumors.

6. Three cases of renal cortex tumors are reported in which preoperative radiation has reduced the size of the tumor.

7. One case of adrenal tumor is reported which was apparently not influenced by preoperative radiation.

8. The immediate effect of reducing the size of the tumor and permitting easier nephrectomy may be a factor in improving the five-year results.

REFERENCES

1. Hyman, A.: Clinical study of malignant tumors of kidney. S. Clin. North America **13**:347 (April) 1933.
2. Judd, E. S., and Hand, J. R.: Hypernephroma. J. Urol. **22**:10 (July) 1929.
3. Smith, G. G.: Neoplasms of kidney and ureter; report of 40 cases. Am. J. Surg. **30**:130 (Oct.) 1935.
4. Smith, G. G., and Shoemaker, A. B.: End result of hypernephroma. J. Urol. **14**:389 (Oct.) 1925.
5. Wharton, L. R.: Preoperative irradiation of massive tumors of kidney; clinical and pathologic study. Arch. Surg. **30**:35 (Jan.) 1935.
6. Mintz, E. R.: Natural history of some renal tumors. New Eng. J. Med. **213**:251 (Aug. 8) 1935.
7. Walker, K.: Prognosis of renal growths. Lancet **1**:565 (March 9) 1935.
8. Waters, C. A.: Preoperative irradiation of cortical renal tumors. Am. J. Roentgenol. **33**:149 (Feb.) 1935.
9. Bothe, A. E.: Effect of roentgen therapy upon tumors of kidney. Am. J. Roentgenol. **33**:529 (April) 1935.
10. Waters, C. A.; Lewis, L. G., and Frontz, W. A.: Radiation therapy of renal cortical neoplasms, with special reference to preoperative irradiation. South. M. J. **27**:290 (April) 1934.

DISCUSSION

DR. HUGH CABOT: We have had a number of cases similar to those Dr. Prather presents. There is a

striking difference clinically and pathologically between the Wilms' tumor and the adult tumor of the parenchyma of the kidney. Dr. Prather refers to them as cortical tumors and then as parenchymal tumors. I am not quite sure that he wishes to convey the impression that he can separate clinically the tumors of the cortex and the tumors of the parenchyma. We have had experience with a group of cases of Wilms' tumor treated by radiation by the so-called Coutard technic. Whether we all really use the Coutard technic I am very doubtful, but at any rate it is certainly a much more effective method than the earlier method. All of the cases of Wilms' tumor showed very striking shrinkage. All but one were converted from an apparently inoperable type to an operable type. One of them, a very massive tumor, changed but little in size but became practically completely calcified and, ten months after exploration, apparently is precisely the same. It feels calcified and the x-ray film shows calcification, or at least some process which interrupts the passage of the rays, in almost the complete outline of the tumor. It was so intimately associated with the under surface of the liver that it seemed to me impossible to remove it. It had not shrunk very much, but its activity had apparently been very much diminished. All the other cases correspond very closely to what Dr. Prather suggests, going from an inoperable state to a very readily operable one.

I think the most striking case is a recent one. A patient came to us after having had, at the hands of a radiologist, an allegedly "complete course" of radiation for a tumor that crossed the midline and perhaps occupied three-fifths of the abdomen. Under further radiation it shrunk so that, at the time of its removal, it was about the size of a cricket ball. Hence, I am not sure that one needs to take seriously the allegation of previous complete radiation. At least one is, I think, permitted in these cases which have not shrunk and which are Wilms' tumors to try a little more x-ray, carried out by people with whose technic you are entirely familiar.

In the group of tumors of the parenchyma, commonly referred to as the hypernephromas (I do not like the word because I do not like its implication), the shrinkage is less striking. In nearly half the cases we have been unable to say that there was any certain change in the tumor as one examined it.

There was one case that we were certain was inoperable, but, as some of the colon became involved, an obstruction resulted. We sidetracked the colon, did a lateral anastomosis, then treated him as effectually as we could and referred him to a radiologist near his home. The patient was an old Frenchman. That was four and one-half years ago. Every Christmas he sends me a card. The growth has apparently been arrested. Unfortunately it was so obviously inoperable and so obviously very malignant that I did not even take a piece of it, so I have no knowledge as to its pathology.

Let me issue a warning in regard to Wilms' tumor. If you undertake to predict how long after x-ray this tumor will have shrunk to its minimum size and tell the patient to return home and come back to you on a certain day, you may easily be wrong. These patients must be under continuous observation. We have one case that we did not keep under close observation. The shrinkage was rapid and we allowed the child to go home for three weeks to let the shrinkage continue. When he came back, the tumor had begun to increase in size and the second series of x-ray treatments were less successful. When you start x-ray treatment and propose to follow it by operation, keep the patient constantly under observation so that you may remove the tumor at what seems to you the time when it is as small as it is going to be.

BLADDER DIVERTICULA WITH REIMPLANTATION OF THE URETER*

BY CLINTON N. PETERS, M.D.†

DIVERTICULA of the bladder may be classified among the more unusual urological conditions. The etiology of the condition is not entirely plain, but we find the cases occurring chiefly in the male sex. There is no question but that bladder neck obstruction and intravesical pressure are the fundamental principles involved in the formation of diverticula, and there may also well be, in certain cases, a congenital weakness of the bladder structure which may predispose it to the formation of the condition.

Pathology starts with a hypertrophy of the muscle fibers of the bladder in an initial effort to overcome bladder neck obstruction. Secondarily, there is a separation of these fibers with a hernia of the mucous membrane through the bladder wall, resulting in the formation of a sac of varying size. The sac contains no muscle fibers and does not empty at micturition. In the course of the progress of the diverticulum, the sac enlarges, may become infected and adherent to the underlying structures and may contain calculi or become malignant. The most common position for the formation of diverticula is at the weaker portion of the bladder wall where the ureters enter and at the urachus which may have failed to close entirely. The number of such diverticula varies greatly. It is not uncommon to encounter several large and a varying number of small sacs in the same patient. Occasionally, when a diverticulum is situated at the site where the ureter enters the bladder, the ureteral opening is gradually pulled into the sac in the process of enlargement and we have, as a complication of the condition, the ureter entering at the bottom of the diverticulum. Where this condition occurs, pressure from the diverticulum upon the ureter or adhesions from the sac may cause partial obstruction with resulting hydronephrosis of the kidney on that side. Relief of the underlying causes of diverticula, such as strieture, bladder neck obstruction and prostatic hypertrophy, does not in any way tend to cure the condition, and surgery must be resorted to.

*Read before the New England Branch of the American Urological Association, Boston, April 23, 1936.

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Surgery of these conditions is of a comparatively recent date. The first case reported was approached extravesically and was done about 1896. In 1902 or 1903 Young reported the first case approached from an intravesical incision. Up to 1915 the number of successfully operated cases was very small. At the present day, the choice of surgical procedure is the operation which Young has so well outlined, and the usual method is to invert the sac and excise it completely.

I report here two cases of multiple bladder diverticula. One was a man, thirty-six years years old, with a definite stricture as the underlying cause. There were three large diverticula, one on each side where the ureters enter the bladder and the third in the region of the urachus. In this case the ureters were not involved and the surgical procedure was carried out with very little difficulty. The results, as you see from the cystogram one year later, were all that could be desired. In the second case, the man was fifty-six years of age and there was no definite bladder neck obstruction that could be demonstrated. Two large diverticula, the one on the left having the ureter enter at the base of the sac, were successfully removed. The left ureter was reimplanted at the site of the excision. The final result, as you can see by the cystogram, is fairly good, although there still exists some hydronephrosis. What the end-result will be of course will depend on whether we have any stricture of the ureter at the site of reimplantation.

In approaching these cases surgically, I have found that suction with glass tubes about the size of the opening of the diverticulum is a great aid in everting the sac. Where a sac is particularly adherent and it is impossible to completely evert it, usually a line of cleavage of the mucous membrane can be established and complete removal of the membrane with freshening of the edges and double suture of the bladder wall and mucous membrane suffices to give an excellent surgical result. Packing the sac of a diverticulum with gauze and approaching extravesically may, in certain cases, aid in bringing about a successful inversion. But, where the sac is situated posteriorly, this is often impossible and, in these cases, the fibrous wall that is usually adherent to the underlying structures is not disturbed and simple removal of the mucous lining and suture of the opening is all that is necessary.

VIRUS PROBLEMS IN DISEASES OF THE NERVOUS SYSTEM*

BY JUANITA THOMPSON, M.D.†

THE literature of the present day is mute evidence of the interest taken in virus diseases involving the nervous system. One notes frequently a wide divergence among investigators in their interpretation of similar experimental and clinical results. Due to this lack of unanimity of opinion, it should be with a critical and conservative attitude that both the clinical and the laboratory worker approach neurotropic virus problems. A keen realization of the desirability of such a viewpoint prompted the present discussion.

Just as, a few years ago, clinicians were prone to explain many obscure maladies by a vitamin insufficiency, so, at the present time, a similar situation would seem to prevail with virus diseases as the chief offender. This is apparent in a tendency among neurologists to attribute to infection with an unknown virus the etiology of certain neurologic conditions where the clinical findings are not definitely analogous to any conventional syndrome known to be affected by a neurotropic virus. While some of these affections may be induced by a virus, such an etiologic factor should be considered only after every other possibility has been excluded. Undoubtedly, repeated bacteriologic study of suitable material, as well as an intensive search for obscure foci of infection, would reveal some cases of bacterial and others of toxic origin. However, the finding of bacteria does not necessarily preclude the presence of a virus since secondary bacterial invasion occurs in the course of certain known virus diseases. Aside from the variety of clinical conditions which fall into the preceding group, a relatively large number of cases is encountered with neurologic findings similar to those of certain established virus diseases. In very few of these cases, however, is a final clinical diagnosis of a specific virus infection of the nervous system not debatable. The basis for disputing such a diagnosis is the same as in bacterial diseases where any number of individuals may present practically the same manifestations effected by different organisms. Because the inadequacy of our methods renders it difficult to isolate and identify a virus from a living patient is not sufficient excuse to make the invasion of the nervous system by a specific virus a final diagnosis which has been based on presumptive clinical evidence.

Like the neurologist, the neuropathologist frequently finds it impracticable to attribute a disease to a specific virus even though adequate postmortem studies have been carried out on

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This work was aided by a grant from the Rockefeller Foundation.

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cases clinically proffered as being of virus etiology. In cases where the clinical evidence favors infection with a nonbacterial agent, the pathologic reactions found in the nervous system might be considered to fall into four principal groups.

The first group is composed of cases which are notable in that the findings are essentially negative, typified particularly in conditions classified as Landry's paralysis without definite evidence of myelitis.[10, 16] The etiology of this group remains obscure except for the apparent bacterial sterility of the nervous tissue in a considerable number of the cases studied.

The second group is comprised of cases which present a response similar to that occurring in association with or following certain known virus diseases or vaccination, as manifest the postinfective and the postvaccinal encephalitides.[16, 22, 50, 52, 74, 75, 80] The most striking histopathologic feature common to the group is perivascular demyelinization. There is no sure evidence concerning the precise etiology of such conditions. Some investigators have suggested the effect as being produced by the virus of the initiatory infection or by the activation of a pre-existing neurotropic virus; others, that the causation lies in an allergic response. It is of interest to note that Rivers and his co-worker[71] have produced demyelinization in monkeys by the repeated intramuscular injection of aqueous emulsions and alcohol-ether extracts of fresh, sterile, normal rabbit brain. The condition so produced was not transmissible to other monkeys.

The third group is composed of cases, in which the lesions are not characteristic of a particular virus, but rather may be induced by a number of different viruses. Such a picture is presented by cases where the reaction is characterized by a variable degree of degeneration, necrosis and proliferation of the neural elements, together with a secondary infiltration of mononuclear cells, predominant in the Virchow-Robin's spaces. This type of pathologic response is exemplified in the similarity of the lesions noted in the nervous system in both the Japanese[55] and the St. Louis[42] epidemics of encephalitis, despite the dissimilarity of the specific causative viruses.[46, 82, 83, 84, 85] Furthermore, the pathologic findings in the foregoing neurotropic virus diseases are usually impossible to differentiate from those of von Economo's disease where the etiology is unknown.[15, 16, 26, 27, 41, 43, 44, 55, 83] Mention should be made of cases where, in similar reactions, there is revealed, as an additional feature, the presence of intranuclear inclusions of a type occurring in diseases produced by certain different viruses. Dawson's case of lethargic encephalitis[12] illustrates the foregoing response; in his photographs, the inclusions resemble those of experimental meningitis or encephalitis induced with the viruses, herpes simplex (in rabbits and Cebus monkeys),[18, 88] "B" (in rabbits and *Macacus rhesus* monkeys)[61, 63, 66] that of salivary gland disease of guinea pigs,[24] of mice[35, 36, 78] or of rats [35, 36] and many others. In cases of this type it is obvious from the preceding remarks that a specific diagnosis from the pathologic findings alone is impossible although the changes would be considered indicative of the presence of a virus by the majority of neuropathologists.

The fourth group consists of cases which can be conclusively diagnosed by the pathologic findings. In such instances the response so far as is known is effected only by a specific virus. Rabies caused by "street virus" exemplifies this type of distinctive histopathologic reaction.[53, 54, 55]

In considering the specificity of certain pathologic responses, problems connected with intracellular inclusions are of interest.[7, 9, 87] Aside from virus diseases of the nervous system where a distinctive histopathologic type of inclusion body serves as an index for accurately diagnosing the specific etiology, as is exemplified in rabies[53, 54, 55, 67] and in Borna disease,[47, 89] some inclusion-bearing cells, as has been previously noted, may be encountered which are not particularly characteristic for any one virus. In addition to this difficulty, some intracellular inclusions may be confused with and sometimes be impossible to differentiate from certain normal and abnormal intracellular elements of analogous structure. Of such a classification are intracellular alterations due to the injection of hypertonic glucose and certain other solutions,[38, 39, 86] postmortem decomposition and imperfect fixation,[11] degenerative changes, especially of the oxychromatic type,[40] plasmosomes,[8] normal granules, the masses described by Scharrer and Gaupp[68] in the nuclei supraopticus and paraventricularis and accumulations of lipiodol[23] and other substances.

Attention is now directed to biologic problems related to the isolation and the identification of viruses capable of attacking cells of the nervous system. The primary difficulty in some of these affections is obtaining specimens suitable for experimentation from the living individual. Illustrative of this point are diseases with no significant systemic phase, where the etiologic agent is transferred directly from the portal of entry to the brain and the cord by the local nerves. The strict neurotropic viruses, those of poliomyelitis,[6, 27] rabies[26, 27] and Borna disease,[47, 89] exemplify this mode of penetration. Such viruses attack the nerve cells directly, multiply therein and bring about necrosis. In conditions of this type, the portal of entry is the most likely site from which to secure material for experimental study. The time at which the

specimen is taken would seem to have an important bearing on the outcome of biologic cultivation. This is borne out by the infrequency with which the virus of poliomyelitis has been demonstrated in specimens from the respiratory tract of contacts and of individuals with the disease.[49] Certain other virus diseases with neurologic involvement differ from the foregoing strictly neurotropic group in that the viruses attack, multiply and produce demonstrable changes in tissues outside the nervous system. In such affections, virus may or may not be detected in the blood at certain times during the course of the experimental disease, as in infections with the virus of equine encephalitis,[28, 76] "B" virus,[61] the virus of louping-ill[14, 19, 59] and others. It is not to be inferred that the presence of a virus in the circulation invariably indicates, in cases which later develop neurologic disorders, that the nervous system was necessarily involved directly through the blood stream, although this may occur by "growth through" the blood-brain barrier[27] or by the rupture of a diseased blood vessel.[72] The more usual belief, supported by a considerable amount of experimental evidence,[26, 27] is that the virus invades the nervous system by the peripheral nerves. Aside from the preceding groups, including neurotropes and pantropes, lymphocytic choriomeningitis is unique in that the causative virus has been isolated from spinal fluid.[57] From the preceding remarks, it will be apparent that, when one is attempting to isolate a virus from a patient, repeated biologic assay of specimens from all probable sources is essential. The possibility that the condition under investigation was induced by a virus, can seldom, if ever, be ruled out entirely on negative experimental results.

The handling of specimens prior to inoculation is important. Inactivation of virus may be due to a lengthy interval between death of the patient and autopsy, prolonged storage in glycerin or fixation in some kinds of glycerin. Aside from the difficulty of maintaining asepsis in the routine preparation of inocula, potency may be lost through insufficient or excessive dilution or through permitting the inocula to stand for some time, especially at room temperature. The latter should be avoided particularly where one is using emulsions of nervous tissue, since the injection of partially autolysed extracts of normal homologous brain has been found to induce paralysis in a considerable percentage of normal rabbits.[25, 71, 74] Filtration[54] of inocula may result in the loss of viruses which are filtrable only under special conditions. Loss of filter-passing viruses will take place if the porosity of the filter employed is smaller than the size of the virus particles or if the electrical charge on both filter and virus is the same. Furthermore, this process may separate out some particular bacteria essential to the activity of the filter-passer.

It is common knowledge that the isolation of a virus is dependent upon the susceptibility of the host to artificial infection. Hence, when one is attempting to demonstrate the presence of virus in specimens from a human case, the finding of a susceptible host is a real problem. The reason lies in the fact that some viruses are species specific, even to the point of being effective only in a single strain of a particular species, while others have a limited host range. In certain instances, another factor determining the susceptibility of the host to artificial infection is the relation between the age of the animal and the site of inoculation employed. In working with the virus of vesicular stomatitis, Sabin and his co-workers[64] have shown that while the young of certain species are susceptible to infection by all routes, nasal instillation and cutaneous inoculation in the majority of mature animals of the same species are ineffective. In contrast, the same mature animals, resistant by these routes, could be affected by intracerebral injection or by injection of the nerve fibre supplying the cutaneous area that had been previously injected. With the preceding facts in mind, negative experimental results, even when one has available virus-containing material, may be attributable to not having injected a suitable host or to having used an undesirable route for inoculation in mature animals of a susceptible species.

Aside from securing in an infinite series of susceptible hosts a consistent reaction similar to that effected by the primary inoculation, some experimental animals show considerable variation in the serial response. In certain instances, where no primary reaction is apparent in the host, rapid serial passage in a particular species may enhance the virulence of the infective agent to the degree of inducing manifestations of disease. The isolation of "B" virus in rabbits[66] attests to the effectiveness of such a procedure. Occasionally, the converse type of response occurs, as evidenced in a primary reaction in the host which either suddenly or gradually disappears over a small number of serial transfers. In most instances, such reactions are difficult to explain even on a purely theoretical basis.

One of the greatest problems in biologic experimentation lies in the presence of an unrecognized spontaneous virus disease in the host. Some of these affections exist in apparently normal animals and become manifest following slight operative interference, such as intracerebral injection or serial passage of infective material to a nonimmune host.[79] As is well known, the results of certain investigations dealing with virus diseases of the nervous system have been either erroneously interpreted due to incidental contamination by such viruses or open to consid-

erable criticism on the same score. To emphasize the importance of spontaneous virus diseases in animals further, one might point to the demonstration of antiviral substances for the viruses, herpes simplex and "B" in many *Macacus rhesus* monkeys,[17, 63] the complications caused by spontaneous lymphocytic choriomeningitis in monkeys in the experiments of Armstrong and Lillie on the St. Louis virus of epidemic encephalitis[3] and the similarity of the lesions found in Theiler's disease of mice,[77] canine distemper,[13] fox encephalitis[21] and others to those of certain virus diseases involving the central nervous system of man.

Following experimental isolation of a virus, inaccurate identification is not uncommon. This is usually due to a lack of knowledge concerning a naturally acquired immunity in the majority of animals of a certain species to the virus under investigation. Inability to produce artificial infection in these animals leads to an inaccurate conception of the host range which is an important factor in classifying a virus. The scope of this particular biologic problem is evident when one recalls the apparent insusceptibility of New World monkeys to poliomyelitis virus[26] and the difficulties encountered in producing "takes" in a considerable number of *Macacus rhesus* monkeys with the viruses, herpes simplex[17, 45, 88] and "B".[63, 66] In addition to the possibility of failing to establish the host range, another complication is related to the possible existence of a variable degree of cross-immunity between a number of different known viruses[29, 51, 60, 62, 73, 81] and the particular virus under study. Owing to such an immunologic relationship, identification by serologic procedures may be misleading.

When it has been decided that a virus derives from specimens secured from patients or at autopsy, one may have difficulty in proving conclusively that the original human affection was produced by this particular agent. Except in individuals, who develop during the course of the disease immune substances for the "experimentally isolated virus", substantiation of its specificity is largely adduced from indirect evidence. In this connection, confirmation is usually based on demonstrating the "recovered virus" to be serologically identical with a virus that has been proved the cause of a similar human disease. However, should a virus be isolated exclusively from material obtained postmortem from a case peculiar in having neither the clinical nor the pathologic findings analogous to those of an established virus disease and in giving no information regarding the possible humoral response prior to death, to advance as indisputable proof that the "recovered virus" induced the human affection would be, without additional evidence, presumptuous. In such an instance, the experimental reproduction in animals of a clinical and a pathologic picture comparable to that found in the human being is the most convincing circumstantial data. Despite inconclusive proof, suggestive findings of the preceding type should be reported, for, by so doing, other workers will be stimulated to investigate similar cases. Eventually, on the experimental data accumulated from a number of different sources, a final conclusion can be reached concerning the specific etiology of the particular human affection involved.

Many problems are related to the production of immunity to virus diseases of the nervous system.[1, 26, 27, 30, 31, 48, 56, 69] As is well known considerable time is required to effect active immunization. In a disease such as rabies, where the incubation period is very long, vaccination can be successfully carried out. However, such a procedure is useless, except for prophylactic purposes, in diseases with a short incubation period. With the latter idea in mind, a considerable number of investigators have suggested the use of inactivated virus for immunization on a large scale. In this connection, a great deal of controversy exists as to the effectiveness and the dangers involved in the use of neurovaccines containing supposedly inactivated virus. Recently this has been exemplified in the lively disputes regarding the Brodie[4, 5] and the Kolmer[32, 33, 34] poliomyelitis vaccines. The important equivocal points brought out respecting so-called inactivated neurovaccines indicate:

(1) It is almost impossible to determine by available methods when a virus is completely inactivated. The limitations of biologic assay are evident when one considers the number of human fatalities occurring in nonepidemic areas following the exhibition of the Brodie and Kolmer neurovaccines.[37]

(2) If a preparation is completely inactivated, the production of immunity through its use is doubtful in most instances.

(3) The amount of neurovaccine required to effect immunity in animals is not always applicable to man.

(4) If immunity should be produced in man by an inactivated neurovaccine, the resistance would be probably of short duration. This is important where vaccines are expensive to make and difficult to administer.

(5) Finally, the exhibition of a vaccine containing nervous tissue is invariably accompanied by the potential danger of postvaccinal encephalitis.[22, 58, 74, 75]

From the preceding remarks, it is obvious that a great many problems need to be solved before the use of inactivated neurovaccines becomes a practical and a safe procedure in the prevention of virus diseases of the nervous system.

In connection with the subject of vaccination one associates the unusual and the untoward sequelae manifest in postvaccinal encephalitis.[22, 74, 75, 80] Since the etiology of this condition is obscure, there can be no specific therapy. Practical experience attests to the fact that vaccination carried out during the first year of life is rarely, if ever, followed by encephalitis. Thus, it behooves one to advocate more strongly vaccination in infancy.

Perhaps, some brief mention should be made of immunizing methods involving the use of neutral mixtures.[56] Such procedures are based on experiments showing that the exhibition of a mixture containing an appropriate amount of serum from a recovered host together with the homologous virus, usually does not produce in a susceptible animal the disease but rather an apparent immunity. Contrastingly, considerable experimental evidence indicates that certain viruses are not killed or inactivated in neutral mixtures; their activity is merely retarded. This has been particularly well demonstrated in Green's in vivo experiments on fox encephalitis[20] in which a large percentage of foxes given neutral mixtures developed the disease after a very prolonged incubation period. From the foregoing experimental evidence, it is apparent that neutral mixtures are potentially dangerous and are impracticable to employ in man.

Problems pertaining to the therapeutic use of antiviral serums in neurotropic virus diseases are of interest.[26, 27, 56] In this connection certain important factors should be considered. In some strictly neurotropic virus diseases, as previously noted, the nervous system is involved from the first, the infective agent being either attached to or within many of the nerve cells. Thus, antibodies introduced into the systemic system must penetrate the hemato-encephalic barrier and the cell membrane to be effective. Under normal conditions the blood-brain barrier is capable of holding back circulating antibodies. Whether the cell membrane is permeable to such complex molecules is not clear. It would seem, therefore, that once a nerve cell is affected by a virus, treatment with antiserum can be of little value. One would think that uninvolved cells might be protected to some extent by antiviral serum. However, if the response in other virus diseases of the nervous system is comparable to that in acute poliomyelitis, protection seems most unlikely. Another noteworthy point relative to therapy with antiviral serums is brought out in studies on equine encephalitis. In the artificial infection in monkeys, it has been shown that, following the appearance of humoral neutralizing antibodies, approximately half of the animals develop encephalitis and die. Such being true in this and in certain other virus diseases involving the nervous system, the uselessness of administering antiviral serum is evident.

Recently, interesting experimental studies dealing with the prevention of certain neurotropic virus diseases have been reported. The work is based on the hypothesis that the transmission of virus to the nervous system, by the olfactory route at least, would be impossible if a block were placed between the nerve endings and the virus. In experiments on acute poliomyelitis in monkeys, an apparently effective barrier was produced by repeated intranasal irrigation of certain chemicals[70] or by the repeated application of alum or tannic acid to the nasal mucosa,[2, 65] since in the majority of animals so treated attempts to induce infection by the nasal route were unsuccessful. However, the experiments cited are in a very preliminary stage. Much more substantiation of this work is necessary before human prophylaxis should be considered.

Some of the practical difficulties that may be encountered in the study of virus diseases of the nervous system have been pointed out and it is hoped that they will emphasize the need of more careful evaluation of clinical and of laboratory data.

REFERENCES

1. Andrewes, C. H.: Immunity in virus diseases. Lancet **1**:989 (May 2); 1046 (May 9) 1931.
2. Armstrong, C. and Harrison, W. T.: Prevention of intranasally-inoculated poliomyelitis of monkeys by instillation of alum into nostrils. Pub. Health Rep. **50**:725 (May 31) 1935.
3. Armstrong, C. and Lillie, R. D.: Experimental lymphocytic choriomeningitis of monkeys and mice produced by the virus encountered in studies of 1933 St. Louis encephalitis epidemic. Pub. Health Rep. **49**:1019 (Aug. 31) 1934.
4. Brodie, M.: Active immunization of children against poliomyelitis with formalin inactivated virus suspension. Proc. Soc. Exper. Biol. & Med. **32**:300 (Nov.) 1934.
5. Brodie, M.: Active immunization in monkeys against poliomyelitis with germicidally inactivated virus. Science **79**:594 (June 29) 1934.
6. Brodie, M. and Elvidge, A. R.: Portal of entry and transmission of the virus of poliomyelitis. Science **79**:235 (March 9) 1934.
7. Cowdry, E. V.: The problem of intranuclear inclusions in virus diseases. Arch. Path. **18**:527 (Oct.) 1934.
8. Cowdry, E. V. and Kitchen, S. F.: Intranuclear inclusions in yellow fever. Am. J. Hyg. **11**:227 (March) 1930.
9. Cowdry, E. V. and Scott, G. H.: Nuclear inclusions in kidneys of Macacus rhesus monkeys. Am. J. Path. **11**:659 (July) 1935.
10. Cecil, R. L.: A Textbook of Medicine. Second Edition. Philadelphia and London: W. B. Saunders Co., 1930.
11. Davenport, H. A.; Ranson, S. W. and Terwilliger, E. H.: Nuclear changes simulating inclusion bodies in dorsal-root ganglion cells. Anat. Record **48**:251, 1931.
12. Dawson, J. R.: Cellular inclusions in cerebral lesions of lethargic encephalitis. Am. J. Path. **9**:7 (Jan.) 1933.
13. Dunkin, G. W. and Laidlaw, P. P.: Studies in dog distemper. J. Comp. Path. & Therap. **39**:201, 213, 1926.
14. Fite, G. L. and Webster, L. T.: Distribution of the virus of louping-ill in the blood and brain of intranasally infected mice. Proc. Soc. Exper. Biol. & Med. **31**:695 (March) 1934.
15. Freeman, W.: Chronic epidemic encephalitis. J. A. M. A. **87**:1601 (Nov. 13) 1926.
16. Freeman, W.: Neuropathology. Philadelphia and London: W. B. Saunders Co., 1933.
17. Gay, F. P. and Holden, M.: Herpes encephalitis problem. J. Infect. Dis. **53**:287 (Nov.-Dec.) 1933.
18. Goodpasture, E. W. and Teague, O.: Experimental production of herpetic lesions in organs and tissues of the rabbit. J. M. Research **44**:121 (Dec.) 1923-24.
19. Gordon, W. S.: Comparative aspects of louping-ill in sheep and poliomyelitis of man. Brit. M. J. **1**:885 (May 19) 1934.
20. Green, R. G.: Development of immunity to fox encephalitis. Am. J. Path. **11**:831, 1935.
21. Green, R. G.; Katter, M. S.; Shillinger, J. E. and Hanson, K. B.: Epizootic fox encephalitis. Am. J. Hyg. **18**:462 (Sept.) 1933.

22. Harvey, W. F. and Acton, H. W.: An examination into the degree of efficacy of antirabic treatment. Indian J. M. Research **10**:1020 (April) 1923.
23. Hirsch, E. F.: Radial inclusions of giant cells. Am. J. Path. **10**:686, 1934.
24. Hudson, N. P. and Markham, F. S.: Brain to brain transmission of submaxillary gland virus in young guinea pigs. J. Exper. Med. **55**:405 (March) 1932.
25. Hurst, E. W.: Effects of injection of normal brain emulsion into rabbits. J. Hyg. **32**:33 (Jan.) 1932.
26. Hurst, E. W.: The neurotrophic virus diseases. Lancet **2**:697, 758 (Sept. 28) 1935.
27. Hurst, E. W.: The newer knowledge of virus diseases of the nervous system. Brain **59**:1 (March) 1936.
28. Hurst, E. W.: Infection of rhesus monkey and the guinea-pig with virus of equine encephalomyelitis. J. Path. & Bact. **42**:271 (Jan.) 1936.
29. Hurst, E. W.: Studies of pseudorabies. J. Exper. Med. **63**:449 (March) 1936.
30. Jungeblut, C. W.: The effect of concentration and of various tissue constituents on the virulence of poliomyelitis virus. J. Immunol. **22**:99 (Feb.) 1932.
31. Jungeblut, C. W.: The mechanism of immunity in experimental poliomyelitis. J. Infect. Dis. **58**:150, 1936.
32. Kolmer, J. A.: Susceptibility and immunity in relation to vaccination in acute anterior poliomyelitis. J. A. M. A. **105**:1956 (Dec. 14) 1935.
33. Kolmer, J. A.: A successful method for vaccination against acute anterior poliomyelitis. J. A. M. A. **104**:456 (Feb. 9) 1935.
34. Kolmer, J. A. and Rule, A. M.: Tests for immunity to acute anterior poliomyelitis; colloidal gold, complement fixation and precipitation tests. J. Immunol. **29**:199 (Sept.) 1935.
35. Kuttner, A. G. and Wang, S. H.: The problem of the significance of inclusion bodies in the salivary glands of infants, and the occurrence of inclusion bodies in the submaxillary glands of hamsters, white mice, and wild rats. J. Exper. Med. **60**:773 (Dec. 1) 1934.
36. Kuttner, A. G. and Tung, T.: Further studies on submaxillary gland viruses of rats and guinea pigs. J. Exper. Med. **62**:805 (Dec.) 1935.
37. Leake, J. P.: Poliomyelitis following vaccination against this disease. J. A. M. A. **105**:2152 (Dec. 28) 1935.
38. Lee, J.: Nuclear changes following intravenous injection of varicus solutions. Proc Soc. Exper. Biol. & Med. **31**:383, 1933.
39. Lee, J.: Nuclear alterations following intravenous injections of sucose and of other solutions. Am. J. Path. **12**:217 (March) 1936.
40. Magalhães, A. deG.: The kidneys in yellow fever. Arch. Path. **11**:561 (April) 1931.
41. Matheson Commission: Epidemic Encephalitis. New York: Columbia University Press, 1929 and 1932.
42. McCordock, H. A.; Collier, W. and Gray, S. H.: Pathologic changes in the St. Louis type of acute encephalitis. J. A. M. A. **103**:822 (Sept. 15) 1934.
43. McIntosh, J.: Encephalitis Lethargica. (Epidemic encephalitis.) System of Bacteriology. M. Research Council **7**:169, 1930.
44. McIntosh, J. and Woodcock, H. M.: The etiology of epidemic encephalitis. Brit. Med. J. **2**:611 (Oct. 1) 1927.
45. McKinley, E. B. and Douglass, M.: Herpes encephalitis in monkeys of genus Cebus, with observations on green streptococcus. J. Infect. Dis. **47**:511 (Dec.) 1930.
46. Muckenfuss, R. S.; Armstrong, C. and Webster, L. T.: The etiology of the 1933 epidemic of encephalitis. J. A. M. A. **103**:731 (Sept. 8) 1934.
47. Nicolau, S. and Galloway, I. A.: Borna disease and enzootic encephalomyelitis of sheep and cattle. M. Research Council, No. 121, 1928-29.
48. Olitsky, P. K. and Cox, H. R.: Experiments on active immunization against experimental poliomyelitis. J. Exper. Med. **63**:109 (Jan.) 1936.
49. Paul, J. R.; Trask, J. D. and Webster, L. T.: The isolation of poliomyelitis virus from the nasopharynx. J. Exper. Med. **62**:245 (Aug.) 1935.
50. Perdrau, J. R.: The histology of post-vaccinal encephalitis. J. Path. & Bact. **31**:17 (Jan.) 1928.
51. Perdrau, J. R.: Australian epidemic of encephalomyelitis. J. Path. & Bact. **42**:59 (Jan.) 1936.
52. Perdrau, J. R. and Pugh, L. P.: The pathology of disseminated encephalomyelitis of dog. J. Path. & Bact. **39**:79 (Jan.) 1930.
53. Rivers, T. M.: Some general aspects of pathological conditions caused by filterable viruses. Am. J. Path. **4**:91 (March) 1928.
54. Rivers, T. M.: Filterable viruses. Baltimore: Williams and Wilkins Co., 1928.
55. Rivers, T. M.: The relation of filtrable viruses to diseases of the nervous system. Arch. Neurol. & Psychiat. **28**:757 (Oct.) 1932.
56. Rivers, T. M.: Pathologic and immunologic problems in the virus field. Am. J. M. Sc. **190**:435 (Oct.) 1935.
57. Rivers, T. M. and Scott, T. F. M.: Meningitis in man caused by filterable virus. J. Exper. Med. **63**:397, 415 (March) 1936.
58. Rivers, T. M. and Schwentker, F. F.: Encephalomyelitis accompanied by myelin destruction experimentally produced in monkeys. J. Exper. Med. **61**:689 (May) 1935.
59. Rivers, T. M. and Schwentker, F. F.: Louping ill in man. Proc. Soc. Exper. Biol. & Med. **30**:1302 (June) 1933.
60. Sabin, A. B.: Studies on B virus; immunological identity of virus isolated from human case of ascending myelitis with visceral necrosis. Brit. J. Exper. Path. **15**:248 (Aug.) 1934.
61. Sabin, A. B.: Studies on B virus; properties of virus and pathogenesis of experimental disease in rabbits. Brit. J. Exper. Path. **15**:268 (Aug.) 1934.
62. Sabin, A. B.: Studies on the B virus; immunological relationships of pseudorabies. Brit. J. Exper. Path. **15**:372 (Dec.) 1934.
63. Sabin, A. B.: Studies on the B virus; experimental disease in Macacus rhesus monkeys. Brit. J. Exper. Path. **15**:321 (Dec.) 1934.
64. Sabin, A. B. and Olitsky, P. K.: Physiological and structural host factors in the peripheral and central nervous system influencing the invasiveness of certain neurotrophic viruses and their possible rôle in the epidemiology of poliomyelitis. Proc. Am. A. Path. & Bact., 1936. (In press.)
65. Sabin, A. B.; Olitsky, P. K. and Cox, H. R.: Protective action of certain chemicals against infection with poliomyelitis virus by the nasal route. J. Bact. **31**:35 (Jan.) 1936.
66. Sabin, A. B. and Wright, A. M.: Acute ascending myelitis following a monkey bite, with the isolation of a virus capable of reproducing the disease. J. Exper. Med. **59**:115 (Feb.) 1934.
67. Schaffer, K.: Beitrag zur Pathologie der menschlichen Lyssa. Ztschr. f. d. ges. Neurol. u. Psychiat. **136**:547, 1931.
68. Scharrer, E. and Gaupp, R.: Neuere Befunde am Nucleus supraopticus und Nucleus paraventricularis des Menschen. Ztschr. f. d. ges. Neurol. u. Psychiat. **148**:766 (Sept.) 1933.
69. Schultz, E. W. and Gebhardt, L. P.: On the problem of immunization against poliomyelitis. California & West. Med. **43**:111 (Aug.) 1935.
70. Schultz, E. W. and Gebhardt, L. P.: Prevention of intranasally inoculated poliomyelitis in monkeys by previous intranasal irrigation with chemical agents. Proc. Soc. Exper. Biol. & Med. **34**:133 (March) 1936.
71. Schwentker, F. F. and Rivers, T. M.: The antibody response of rabbits to injections of emulsions and extracts of homologous brain. J. Exper. Med. **60**:559 (Nov.) 1934.
72. Seifried, O.: Histological studies on hog-cholera; lesions in central nervous system. J. Exper. Med. **53**:277 (Feb.) 1931.
73. Shope, R. E.: Experiments on the epidemiology of pseudorabies. Am. J. Path. **11**:838, 1935.
74. Stuart, G. and Krikorian, K. S.: Anti-rabic procedure in Palestine with special reference to decentralization and treatment. Ann. Trop. Med. **19**:399 (Dec.) 1925.
75. Stuart, G. and Krikorian, K. S.: Fatal neuroparalytic accident of antirabies treatment. Lancet **1**:1123 (May 24) 1930.
76. Ten Broeck, C. and Merrill, M. H.: Transmission of equine encephalomyelitis by mosquitoes. Am. J. Path. **11**:847, 1935.
77. Theiler, M.: Spontaneous encephalomyelitis of mice. Science **80**:122 (Aug. 3) 1934.
78. Thompson, J.: Salivary gland disease of mice. J. Infect. Dis. **58**:59 (Jan.-Feb.) 1936.
79. Thompson, J.: Spontaneous virus diseases in common laboratory animals. Arch. Path. (In press.)
80. Turnbull, H. M.: Encephalo-myelitis in virus diseases and in exanthemata. Brit. M. J. **2**:331 (Aug. 25) 1928.
81. Watson, E.: Discussion of R. G. Green's paper. (See reference 20.) Am. J. Path. **11**:831, 1935.
82. Webster, L. T. and Fite, G. L.: Virus encountered in the study of material from cases of encephalitis in St. Louis and Kansas City epidemics of 1933. Science **78**:463 (Nov. 17) 1933.
83. Webster, L. T. and Fite, G. L.: Contribution to the etiology of encephalitis. Differentiation of encephalitis by protection tests. Proc. Soc. Exper. Biol. & Med. **31**:344 (Dec.) 1933.
84. Webster, L. T. and Fite, G. L.: Serological relationship of St. Louis and Japanese encephalitis. Am. J. Path. **10**:667, 1934.
85. Webster, L. T. and Fite, G. L.: Experimental studies on encephalitis. J. Exper. Med. **61**:103 (Jan.); 411 (Mar.) 1935.
86. Weed, L. H. and McKibben, P. S.: Experimental alteration of brain bulk. Am. J. Physiol. **48**:531 (Mar. 22) 1919.
87. Wolf, A. and Orton, S. T.: Occurrence of intranuclear inclusions in human nerve cells in a variety of diseases. Bull. Neurol. Inst. N. Y. **2**:194 (July) 1932.
88. Zinsser, H.: Herpes encephalitis in Cebus monkeys. J. Exper. Med. **49**:661 (April) 1929.
89. Zwick, W.; Seifried, O. and Witte, J.: Weitere Beiträge zur Erforschung der Bornaschen Krankheit des Pferdes. Arch. f. wissensch. u. prakt. Tierh. **59**:511 (June 18) 1929.

A COMPARISON OF ACCURACY IN THE DIAGNOSIS OF SINGLE AND MULTIPLE VALVULAR DISEASE OF THE HEART*

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MANY physicians, competent in the diagnosis of valvular disease of the heart, commit themselves as to the specific lesions with some reluctance when two or more of the valves are thought to be involved. The belief that our diagnostic ability is limited in multiple valvular disease has become rather firmly rooted in the minds of many practitioners and teachers, to the extent that in some quarters there is great hesitancy in diagnosing with certainty even the common combination of mitral stenosis with aortic insufficiency. We are not aware of any evidence in support of this belief, and a review of the literature has revealed no correlation of antemortem diagnoses with postmortem findings directly concerned with this question. This note is concerned with an effort to establish the truth or falsity of the belief.

All cases of chronic rheumatic valvular disease examined postmortem at the Peter Bent Brigham Hospital were reviewed, and the clinical diagnoses were correlated with the anatomic findings (except that the great number of uncomplicated cases of mitral stenosis made it unnecessary to review more than a part of them). Cases were freely excluded when the actual existence of stenosis or insufficiency was debatable anatomically, so that the series cannot be taken to represent the comparative incidence of the various combinations. Only a few examples of aortic insufficiency are included, largely because we often found great difficulty in convincing ourselves, from the descriptions, that there had actually been regurgitation of blood. We have not regarded the "water test" for aortic regurgitation as a reliable guide to the presence or absence of this lesion.

In grouping the cases we have regarded stenosis as the major lesion for a given valve, and have disregarded the additional presence of insufficiency of that valve. Insufficiency in the absence of stenosis, however, has not been disregarded. We have compared, for example, cases of aortic stenosis (with or without insufficiency) in which the other valves were normal with cases in which this lesion was combined with stenosis or insufficiency of one or more of the other valves. The same process was repeated for the mitral valve. There were no cases in which the tricuspid valve was involved

TABLE 1

NUMBER OF CASES IN EACH COMBINATION AND NUMBER CORRECTLY DIAGNOSED

	Cases Seen by the General Service					Cases Seen by Experts					Cases Seen by Experts. Moribund Cases Excluded				
	Number Seen	Number Correctly Diagnosed				Number Seen	Number Correctly Diagnosed				Number Seen	Number Correctly Diagnosed			
		AS	AI	MS	MI		AS	AI	MS	MI		AS	AI	MS	MI
AS	45	18	—	—	—	23	11	—	—	—	17	9	—	—	—
AI	10	—	10	—	—	7	—	7	—	—	6	—	6	—	—
MS	24	—	—	18	—	16	—	—	14	—	14	—	—	13	—
MI	16	—	—	—	8	8	—	—	—	3	7	—	—	—	3
AS & MS	33	17	—	24	—	18	11	—	14	—	15	10	—	12	—
AS & MI	3	1	—	—	1	3	2	—	—	1	2	2	—	—	0
AI & MS	8	—	6	7	—	5	—	4	4	—	5	—	4	4	—
AI & MI	5	—	5	—	3	4	—	4	—	3	4	—	4	—	3
MS & TS	6	—	—	5	—	3	—	—	2	—	3	—	—	2	—
MS & TI	3	—	—	1	—	3	—	—	1	—	1	—	—	1	—
MI & TI	2	—	—	—	0	1	—	—	—	0	1	—	—	—	0
AS, MS & TS	13	6	—	12	—	10	6	—	9	—	8	5	—	8	—
AS, MS & TI	4	2	—	3	—	3	2	—	3	—	3	2	—	3	—
AS, MI & TI	1	0	—	—	0	0	—	—	—	—	0	—	—	—	—
AI, MS & TS	2	—	1	2	—	2	—	1	2	—	2	—	1	2	—
AI, MS & TI	2	—	2	2	—	2	—	2	2	—	2	—	2	2	—

"A" means aortic; "M", mitral; "T", tricuspid; "S", stenosis; and "I", insufficiency. Thus, "AS" means aortic stenosis; "TI", tricuspid insufficiency, and so forth.

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Aided by a grant from the Proctor Fund of Harvard University for the Study of Chronic Diseases.

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alone, and none in which there was deformity of the pulmonic valve great enough to produce stenosis or insufficiency. We are, therefore, limited to a comparison of accuracy in single with that in combined aortic and mitral disease.

TABLE 2

PERCENTAGE OF CASES IN WHICH AN ACCURATE DIAGNOSIS WAS MADE

	By the General Service	By Experts	By Experts, Moribund Cases Excluded
AS uncomplicated	40	47.8	52.9
AS complicated	60	61.8	67.9
AI uncomplicated	100	100	100
AI complicated	82.4	84.6	84.6
MS uncomplicated	75	87.5	92.9
MS complicated	78.9	80.4	87.2
MI uncomplicated	50	37.5	42.9
MI complicated	36.4	50	42.9

In making the clinical correlations, we have reviewed the diagnoses made by the hospital staff as a whole, and have considered separately those cases seen by some member of the staff we consider particularly adept in cardiovascular diagnosis. From this last group we have made still another correlation after eliminating cases which were moribund on admission (cases in which reasonable accuracy in diagnosis could hardly be expected).

Table 1 shows the number of cases in each group, together with the number correctly diagnosed, and table 2 shows the accuracy of diagnosis in percentages. It is evident that accuracy in the diagnosis of aortic stenosis was better when this lesion existed in the presence of deformity of other valves than when the aortic valve alone was involved. In the case of insufficiency of the aortic valve, the reverse is true. Mitral stenosis was diagnosed with approximately the same accuracy with and without deformity of other valves. Insufficiency of the mitral valve without stenosis was also diagnosed with essentially the same accuracy whether or not other valves were deformed.

Comment: It is particularly significant that mitral stenosis was correctly diagnosed with approximately the same accuracy whether other valves were deformed or not. The same accuracy obtained even in the presence of aortic insufficiency, a fact which tends to diminish the importance of the Austin Flint murmur as a factor leading to error in the diagnosis of mitral stenosis. It is probable that unless the aortic insufficiency is of marked degree, the long rumbling low-pitched diastolic murmur at the apex is as indicative of mitral stenosis as it is when aortic insufficiency is absent.

The better recognition of aortic stenosis in the combined form is possibly due to the fact that many of the combined cases were associated with mitral stenosis, a lesion overlooked with comparative rarity, and that when disease is found in one valve, the examiner is likely to search exhaustively for involvement of other valves. We are often inclined to dismiss, as unimportant, systolic murmurs heard at the base of the heart; but when mitral stenosis is known to be present, we are perhaps likely to search more carefully for the confirmatory aortic systolic thrill.

Summary and Conclusions: This correlation of clinical diagnoses with postmortem findings has shown, first, that the diagnosis of aortic stenosis is more accurate when the lesion exists in combination with deformity of other valves than when the other valves are normal; secondly, that the diagnosis of aortic insufficiency is less accurate when other valves are also involved; thirdly, that the condition of the other valves makes no material difference in the accuracy with which lesions of the mitral valve are recognized. This series lends no support, then, to the common belief that diagnostic accuracy is poorer in combined valvular disease than it is in uncomplicated deformity of but a single valve, except in the case of aortic insufficiency.

DO YOU KNOW?

The first law to regulate the practice of medicine in the colonies was passed in Massachusetts in 1649; a similar act was made law in New York State, 1665.

Alexander the Great, Persius and Terence died just under or over thirty years of age. Keats, Shelley and Schubert had their careers cut short. How little this really proves is shown by the fact that the average age at death of the eminent men of antiquity was 66.7 years, while in modern times, 82 noted mathematicians averaged 64.3, 75 poets 64.1, and all the presidents of the United States 68.4. The figures so often cited about increasing the "expectation of life" and supposed to prove this or that, refer to expectation at time of birth. This increase is the result of removing many of the perils of infancy and early childhood. In the modern era more babies grow up to maturity than before, but among people who arrive at maturity the average do not live to die at a greater age than formerly.

CONTRIBUTIONS TO AID IN RESEARCH RELATING TO CLINICAL MEDICINE

The Committee on Scientific Research of the American Medical Association invites applications for grants of money to aid in research on problems bearing more or less directly on clinical medicine. Preference is given to requests for moderate amounts to meet specific needs. For application forms and further information, please address the committee at 535 North Dearborn Street, Chicago.—*Science* 84:244 (Sept. 11) 1936.

VERMONT STATE MEDICAL SOCIETY

The One Hundred and Twenty-Third Annual Meeting of the Vermont State Medical Society will be held at the Fleming Museum Auditorium, Burlington, Vermont, Thursday and Friday, October 15 and 16, 1936.

Officers for 1935-1936

President: Lester W. Burbank, Cabot.
Vice-President: John Trotter, Jr., Bennington.
Secretary: William G. Ricker, St. Johnsbury.
Treasurer: David Marvin, Essex Junction.
Auditor: E. H. Buttles, Burlington.
Councilors: 1st District: E. A. Hyatt, St. Albans; 2nd District: C. M. Campbell, Manchester Center; 3rd District: F. E. Farmer, St. Johnsbury; 4th District: J. H. Woodruff, Barre.
Executive Committee: B. F. Cook, Rutland; W. G. Ricker, St. Johnsbury; A. B. Soule, Burlington.
Publication Committee: W. G. Ricker, St. Johnsbury; C. F. Dalton, Burlington; A. M. Cram, Bridgewater.
Legislative Committee: C. H. Beecher, Burlington; E. J. Quinn, Castleton; E. A. Tobin, Bennington.
Medical Education: S. W. Hammond (1), Rutland; S. S. Eddy (2), Middlebury; N. R. Caldwell (3), Burlington.
Necrology Committee: B. D. Adams, Burlington; G. G. Marshall, Rutland; H. L. Pierce, Swanton.
Medico-Legal Committee: F. E. Farmer (1), St. Johnsbury; E. A. Hyatt (2), St. Albans; J. N. Jenne (3), Burlington.
Health and Public Instruction: F. J. Lawliss, Richford; A. B. Soule, Burlington; Stewart Ross, Rutland; A. B. Woodman, Springfield; E. H. Buttles, Burlington.

Delegates

Maine: L. R. Goodrich, Vergennes.
New Hampshire: G. B. Hyde, Wilmington.
Massachusetts: G. R. Anderson, Brattleboro.
Connecticut: L. H. Ross, Bennington.
Rhode Island: A. L. Fogg, Burlington.
New York: L. E. Sample, St. Albans.
American Medical Association: W. G. Ricker, St. Johnsbury.
Alternate: C. H. Beecher, Burlington.
Anniversary Chairman: O. N. Eastman, Burlington.
Members of New England Medical Council: J. H. Woodruff, Barre; G. G. Marshall, Rutland; W. G. Ricker, St. Johnsbury; J. A. Stevenson, Chester; E. A. Hyatt, St. Albans.
Nominating Committee: George B. Hyde, Wilmington; F. J. Lawliss, Richford; Frank C. Phelps, Vergennes.

Local Committee of Arrangements

A. G. Mackay, Chairman; E. L. Amidon; B. F. Clark.
Ladies Committee: Mrs. W. T. Rees, Chairman.
Reception Committee: Mrs. P. K. French, Chairman.
Luncheon Committee: Mrs. Sam Sparhawk, Jr., Chairman.
Bridge Committee: Mrs. K. C. McMahon, Chairman.
Transportation: Mrs. A. G. Mackay.

Officers of the House of Delegates

President: F. J. Lawliss, Richford.
1st Vice-President: Ralph Seeley, Rutland.
2nd Vice-President: E. D. McSweeney, Burlington.
Secretary: E. J. Rogers, Pittsford.

Wednesday evening, October 14, 8 p. m. Preliminary Meeting of House of Delegates on the Roof Garden of the Hotel Vermont.

Thursday afternoon, October 15, 1 p. m. Regular session of House of Delegates at Fleming Museum.

All delegates must present credentials signed by the President and Secretary of their respective County Societies.

Program

Thursday Forenoon, October 15, 1936, at nine-thirty o'clock at the Fleming Museum

1. Call to Order by the President—L. W. Burbank, M.D., Cabot.
2. Invocation—Rev. William Fisher Lewis.
3. Address of Welcome—President Guy W. Bailey, University of Vermont.
4. Reports of the Officers and Committees.
5. Reception of Delegates from other Societies.
6. Vice-President's Address — John Trotter, M.D., Bennington.
   Title: "The Trend of Medical Practice as I See It Today."
7. Address — Doris A. Murray, M.D., Washington, D. C., Children's Bureau, Department of Labor.
   Title: "Maternal and Child Health and Crippled Children's Programs Under the Social Security Act."
8. Paper—Franklin P. Lowry, M.D., Newton, Massachusetts, Consultant in Education of Physical Therapy of the American Medical Association; Instructor in Physical Therapy at Sargent College of Physical Education, Medical School of Boston University and Tufts College Medical School.
   Title: "The Value of Physical Therapy in the Practice of Medicine."
9. Announcements by Exhibitors of Scientific Specimens.
10. Paper — A. D. Rood, M.D., Springfield, Massachusetts; Associate Professor of Bronchoscopy, University of Vermont, College of Medicine; Consulting Bronchoscopist to Mary Fletcher Hospital, Burlington, Westfield Tuberculosis Sanatorium, Cooley Dickinson Hospital, Northampton, Massachusetts.
    Title: "Postoperative Pulmonary Atelectasis."

Thursday Afternoon

Meeting of the House of Delegates at 1 o'clock in the Fleming Museum Auditorium.

List of members, reports of the committees and order of business are printed in pamphlet form. Copies may be obtained at the registration desk.

Two o'clock

11. President's Address — L. W. Burbank, M.D., Cabot.
12. Address—J. H. J. Upham, M.D., Columbus, Ohio, President-Elect of American Medical Association.
    Title: "Heart Disease in Middle and Past-Middle Life."
13. Paper—Guy L. Hunner, M.D., Baltimore, Maryland, Professor of Gynecology, Johns Hopkins University School of Medicine.
    Title: "The Urinary Tract in Relation to Diagnosis of Abdominal and Pelvic Lesions."
14. Address—R. R. Sayers, M.D., Washington, D. C., Medical Officer in Charge of Industrial Hygiene, United States Public Health Service.
    Title: "Silicosis and Similar Dust Diseases."

Thursday Evening at Seven o'clock at the Ethan Allen Club

The Annual Banquet.

Anniversary Chairman, O. N. Eastman, M.D., Burlington.

Friday Forenoon, Nine o'clock at the Fleming Museum

15. Report of the House of Delegates.
16. Symposium — Arranged by Reginald H. Smithwick, M.D., Boston, Mass.

"Medical Aspects of Vascular Disease." Robert S. Palmer, M.D., Boston, Assistant in Medicine at Massachusetts General Hospital; Instructor in Medicine at Harvard Medical School.

"General Management and Treatment of Peripheral Vascular Lesions in Diabetics and Non-Diabetics." Theodore C. Pratt, M.D., Boston, Assistant in Surgery at Massachusetts General Hospital; Assistant in Surgery in Courses for Graduates at Harvard Medical School.

"Special Methods of Treatment of Peripheral Vascular Lesions (Discussion of Passive Vascular Exercises, Peripheral Nerve Block, Embolectomy, etc.)." Robert R. Linton, M.D., Boston, Assistant Surgeon at Massachusetts General Hospital; Instructor in Surgery at Harvard Medical School.

"Present Methods of Treating Varicose Veins." Henry H. Faxon, M.D., Boston, Assistant Surgeon at Massachusetts General Hospital; Assistant in Surgery at Harvard Medical School.

"The Value of Sympathectomy in the Treatment of Vascular Disease (Raynaud's Disease, Angina Pectoris, Essential Hypertension)." Reginald H. Smithwick, M.D., Boston, Assistant Surgeon at Massachusetts General Hospital; Assistant in Surgery at Harvard Medical School.

ENTERTAINMENT

The doctors will have golf privileges at the Country Club on payment of a small Greens Fee.

LADIES' ENTERTAINMENT

The Athena Club will be open Thursday morning for the Visiting Ladies.

Luncheon will be served at the Athena Club, 328 Pearl Street, at 1 p. m., Thursday, October 15. Visiting ladies and wives of Burlington doctors are invited to be guests of the State Medical Society.

Following lunch there will be bridge at the Athena Club for any who wish to play.

NOTES

The Headquarters of the Society and Registration Desk will be in the Foyer of the Fleming Museum on Colchester Avenue. Banquet tickets should be purchased when registering.

BY-LAWS

Article IX—Time for Papers

No author shall consume more than twenty minutes in reading or presenting a paper and no one shall speak more than five minutes in the discussion of a paper, without unanimous consent of the members present.

Article X—Addresses Property of Society

All addresses and papers presented in the County and State Societies thereby become the property of the State Society, and shall be placed in the hands of the Secretary within one week after the meeting, for insertion in the Records.

Article XI—Order of Business

The program as prepared by the Executive Committee and published in accordance with the By-Laws by the Secretary shall constitute the order of business, and cannot be changed, or suspended, except for a definite purpose, a limited time and by a two-thirds vote of the members present.

SCIENTIFIC EXHIBITORS

Dr. W. B. Fitch, St. Johnsbury
Dr. D. E. Sheffield, St. Johnsbury
Dr. W. R. Harkness, Montpelier
Dr. R. E. Avery, Barre
Dr. Wilmer Angell, Randolph
Dr. Leslie Sycamore, Hanover, N. H.
Dr. B. F. Cook, Rutland
Dr. E. J. Rogers, Pittsford
Dr. L. E. Sample, St. Albans
Dr. R. H. Seeley, Rutland
Dr. C. S. Leach, Brattleboro
Dr. N. R. Caldwell, Burlington
Dr. A. B. Soule, Jr., Burlington.

COMMERCIAL EXHIBITORS

Elmer N. Blackwell
Cameron Surgical Specialty Company
Otis Clapp & Son
Davies, Rose & Co., Ltd.
The Denver Chemical Mfg. Company
Endo Products, Incorporated
George C. Frye Company
General Electric X-ray Corporation
High Tension Corporation
Lederle Laboratories, Incorporated
E. F. Mahady Company
E. H. Marcy Drug Company
Moore & Company, Incorporated
C. V. Mosby Company.
P. J. Noyes Company
Philip Morris & Company, Ltd.
R. J. Strasenburgh Company
Surgeons' and Physicians' Supply Company.

MISCELLANY

VERMONT DEPARTMENT OF PUBLIC HEALTH

AUGUST, 1936

The following communicable diseases were reported to the office of the Department of Public Health during the month of August: whooping cough 96; mumps 20; chickenpox 20; undulant fever 4; scarlet fever 11; measles 5; German measles 7 and diphtheria 1.

The Laboratory of Hygiene made 2,007 examinations, the details of which are as follows:

Examinations for diphtheria bacilli	89
" " Widal reaction for typhoid fever	57
" " undulant fever	83
" " gonococci in pus	176
" " tubercle bacilli	173
" " syphilis	602
" of water, chemical and bacteriological	221
" " water, bacteriological	341
" " milk, market	142
Examinations of milk, submitted for chemical only	0
" " milk, submitted for microscopical only	9
" " foods	2
" " drugs	0
" for courts, autopsies	7
" " courts, miscellaneous	30
Autopsies to complete death returns	4
Other Examinations	71
Total Examinations	2,007

The Director of the Division of Venereal Diseases reports 56 cases of gonorrhea and 65 cases of syphilis made to the Division in August. Six hundred and twenty-five Wassermann outfits and 334 slides for gonorrhea were distributed from this Division.

The Crippled Children's Division reports 100 patients seen at their homes, 503 at clinics and 4 at the Burlington office making a total of 607 patients. One patient was admitted and one discharged from the Massachusetts General Hospital and one patient was discharged from the Rutland Hospital. Twelve pieces of apparatus were altered or repaired and forty-four orthopedic corrections were made to shoes. The Vocational Worker of this Division reports sales made amounting to $222.87.

The Director of the Maternal and Child Health Division reports that he assisted in the examination of children at the summer round-up held at Waits River, and also that he attended the meeting of the Franklin County Medical Society. A dentist has been engaged for this Division and is to start work September 1.

The Public Health Nursing Division reports seven nurses now in the field, with health centers established at Wallingford, Randolph Center and Bolton-ville. The WPA Nursing Projects are being continued and more nurses added as schools open. Six hundred and thirty-one notifications of birth registration, 260 diphtheria consent cards and 560 baby booklets were mailed out during the month of August.

THE AMERICAN MEDICAL EDITORS' AND AUTHORS' ASSOCIATION

The American Medical Editors' and Authors' Association is most anxious to bring about a closer relationship between authors and publishers. The Director wishes to announce that articles on medical subjects may be submitted to him for editing and putting into shape for publication. This service will be rendered free of charge. If the manuscript submitted has any real value, with the author's consent, it will be submitted to some medical journal in his neighborhood for publication.

It is sincerely to be hoped that medical men, particularly those who have hesitated to publish articles in the past, will take advantage of this offer. The author need not be a member of the Association.

The largest medical library in the United States is in the Surgeon General's office. The second largest, we believe, is in the New York Academy of Medicine. The services of the Academy library are available at all times. The American Medical Editors' and Authors' Association, through its Director, Dr. Harold Hays, 133 East 58th Street, New York City, can arrange to supply references or abstracts on any medical subject. This service is available to any doctor. Please write to Dr. Hays for information if you are interested. The cost will depend upon how much information is desired. The original bill rendered by the Academy will be sent to the physician making inquiry. The Association makes no charge. This is but one of the services that this Association wishes to render to doctors.

Address all manuscripts to Dr. Harold Hays, Director of the American Medical Editors' and Authors' Association, 133 East 58th Street, New York City.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 22411

PRESENTATION OF CASE

A sixty-eight year old native businessman was admitted complaining of vomiting.

The patient was quite drowsy when first seen and the history was obtained with considerable difficulty for he did not respond very coherently. About one year before entry he first noted that he was losing weight. This progressed up to his entrance to the hospital. About a month before admission his friends commented upon the fact that his skin was yellow, a condition which persisted for about one week and then disappeared. Ten days before entry the skin again became yellow for two to three days. A physician who saw him originally said that he had no jaundice. During these attacks he said that his urine had been darker than normal but he had noticed no change in the color of his stools. For about a month he had become increasingly more constipated and stated that he had no bowel movement for a week prior to entry. He had considerable pruritus currently and had been hiccoughing for about seven to ten days. Ten days before coming to the hospital he began to vomit "brownish material" following the ingestion of any food. He had anorexia and took fluids only in very small quantities. No complaint of pain was elicited from the patient although his housekeeper claimed that he had an attack of constant severe right upper quadrant pain five weeks and again eight days before admission. The initial attack lasted about five days and was only partially relieved by morphine. For about five days he exhibited generalized twitching.

Physical examination showed an elderly, sick looking, drowsy man, hiccoughing and exhibiting frequent twitching of the left arm. There was evidence of considerable weight loss and there were numerous scratch marks on the skin. The skin was pallid and there was no evidence of icterus. The pupils were small, slightly irregular, and reacted sluggishly to light. The tongue was dry and had a heavy grayish-brown coating. The throat was reddened and dry. The heart extended 12 centimeters to the left of the midsternal line. An occasional premature beat was audible and there was a soft blowing systolic murmur at the apex. The blood pressure was 160/60. Bronchovesicular breath sounds were audible at both bases, where also numerous fine moist râles were heard. The abdomen was obese and distended and the flanks were full. Tympany was elicited over an area 10 centimeters in diameter in the region of the umbilicus. A questionable shifting dulness in the right flank was demonstrated, and in the region of the cecum a large, cyst-like tympanitic mass was felt. Peristaltic sounds were present but diminished in intensity. Liver dulness of both left and right lobes extended three finger-breadths beneath the costal margin. The patient did not complain of pain and no localized spasm was demonstrated. A rectal examination showed an enlarged smooth prostate but was otherwise negative.

The temperature was 97°, the pulse 90. The respirations were 20.

Examination of the urine showed a specific gravity of 1.010 with a slight trace of albumin. The sediment contained 36 white blood cells but the examination was otherwise negative. The blood showed a red cell count of 4,600,000, with a hemoglobin of 80 per cent. The white cell count was 17,800, 95 per cent polymorphonuclears. A stool specimen gave a three plus reaction to the guaiac test and fluid from a gastric lavage gave a one plus reaction. The non-protein nitrogen of the blood was 190 milligrams. A carbon dioxide combining power was 42.2 volumes per cent. The chlorides were equivalent to 87 cubic centimeters N/10 sodium chloride per 100 cubic centimeters. A blood sugar of 208 milligrams was obtained six hours after 1,200 cc. of 10 per cent glucose had been administered intravenously.

An x-ray of the abdomen showed a markedly dilated cecum and considerable gas in the small bowel. The transverse colon contained a moderate quantity of gas. A barium enema was expelled almost as rapidly as it entered the bowel, but it was possible to outline the greater part of the colon. There was a large rounded defect in the rectum which resembled a fecolith. The sigmoid was small, rather spastic, and appeared to contain several small diverticula. The ascending colon showed a constant constriction at about the crest of the ilium and in this region were what appeared to be filling defects. The cecum was unusually long and markedly dilated. A chest film showed an enlarged heart and wide mediastinum. The diaphragm was high. There was an oval area of density just above the right diaphragm and the right lung root was larger than the left. There was limited excursion of the right leaf of the diaphragm

and both bases showed diminished radiance.

The patient was treated supportively for three days, during which time the chlorides rose to 103 and the nonprotein nitrogen was lowered to 150 milligrams. The patient seemed much improved and for the first time complained of tenderness in the right flank, which appeared to bulge somewhat. With apparent improvement his white cell count rose to 30,000, and on the third hospital day a laparotomy was performed.

Notes on the History

Dr. Edward L. Young, Jr.: Vomiting, I think, is something like our school friend Gaul; very roughly it is divided into three parts: toxic, obstructive and irritative, generally a mixture.

The picture extends back over a year, with loss of weight, intermittent attacks of jaundice, two attacks of right upper quadrant pain severe enough to need morphia and not to be entirely relieved by it. The story of past symptoms points toward a toxic condition, biliary in origin.

"The abdomen was distended and the flanks were full." Here is evidence of some process in the abdomen which must have produced a considerable degree of fluid. There is nothing so far to suggest a localized septic process, that is no spasm or tenderness and no pain that the patient complained of. The temperature backs that up. It was subnormal, 97°. The pulse was 90, and the respirations 20.

Assuming that we are considering malignancy this is a surprisingly good blood picture for a man who has been losing weight from that cause over a period of a year.

"The white cell count was 17,000, 95 per cent polymorphonuclears." That is the first suggestion of some septic process.

"A carbon dioxide combining power was 42.2 volumes per cent." He is getting toward the level of acidosis.

A one plus guaiac from gastric lavage is not of serious importance. A three plus guaiac in the stool probably means something important going on in the bowel.

"An x-ray of the abdomen showed a markedly dilated cecum and considerable gas in the small bowel." I assume that is a flat plate and spells obstruction of some type.

"A barium enema was expelled almost as rapidly as it entered the bowel, but it was possible to outline the greater part of the colon." I shall ask Dr. Hampton to speak of this, but, if that is true we cannot be dealing with an acute obstruction low in the large intestine. I am going to ask Dr. Hampton if he will not help me out. So far, I find some features suggestive of malignancy and others suggestive of an acute septic process, possibly gallbladder.

X-ray Interpretation

Dr. Aubrey O. Hampton: I remember this patient very well. I did the examination. I was asked if I was perfectly certain this was an intrinsic tumor of the bowel. I said, "Yes; I would be, if I could rule out fecolith." There was one in the rectum and it may be logical to suppose he had one higher up but that would not account for the constriction. The constriction in one of these plates is consistent with an intrinsic lesion, but in this other view it is not quite what you would expect.

Here is the chest taken back down, so of course everything we see is magnified, but there is a shadow above the right side of the diaphragm with diminished radiance, more on the right. The right leaf of the diaphragm did not move so well as the left. The remark about the lung root I think you can discount because we see very little of the lung root due to the magnified aorta.

Differential Diagnosis

Dr. Young: It seems to me we will have to make two or three diagnoses here to account for the whole picture. We cannot have a diagnosis that will fit everything perfectly. First, is this an intestinal obstruction due to the lesion described here? Certainly we can throw out any obstruction from a lesion in the sigmoid. It is perfectly possible that this man has a lesion in the cecum which has gone on and has now perforated, with abscess formation, which will account for the increased white count, the tenderness, and the mass in the right flank. If there is obstruction, that will account for the high nonprotein nitrogen and his vomiting. Then the final white count and tenderness and mass could go with a perforation of carcinoma of the cecum.

What about his jaundice and the evidence of trouble in the gallbladder, and the elevated and fixed diaphragm? It is perfectly possible of course that he has a process which might be malignant in the biliary tract and that that has gone on to perforation. I question a subdiaphragmatic abscess, but at the same time I cannot rule it out. I do not see how I can fit all this picture into disease of the biliary tract or under one diagnosis. It would be very unusual for a metastatic process from the biliary tract to jump down to the right iliac fossa and cause any such picture as that, and it is equally difficult to imagine a primary cecal lesion spreading in such a way as to cause these attacks of transient pain and jaundice. I prefer to assume there may be two separate diseases, old chronic gallbladder with stones and cholangitis, or a slowly growing malignancy in the cecum with obstruction, and with a terminal perforation. I believe there was nothing to do but put in some

novocain and see if drainage of the cecum and drainage of the abscess were possible.

DR. TRACY B. MALLORY: Dr. Young has received one of these left-handed compliments of being given a nearly impossible case. I think it is fair to say that the surgical service did not have a much more definite idea as to what was wrong with the patient than Dr. Young did.

CLINICAL DISCUSSION

DR. OLIVER COPE: I am much encouraged to find that Dr. Young has come to nearly the same conclusions that I did. Before operation I was very much perplexed about the diagnosis. When this patient entered the hospital he was moribund. He improved considerably with intravenous water, salt and glucose. With this improvement, tenderness became apparent in the right flank. After three days a definite mass was palpable. I believe that when he first arrived he was too sick to feel the pain. The patient himself was unable to give a history and the reports we got from friends were conflicting and confusing. I operated on him under a mistaken diagnosis. I thought he probably had a malignancy of the hepatic colon which had perforated, giving him an abscess in the flank. In spite of air visible by x-ray in the transverse colon I operated with the idea of relieving the pressure in his cecum, which was obviously dilated both by x-ray and abdominal palpation. I was afraid the obstruction was complete and the cecum might blow out. Fortunately I made a right rectus incision and an adequate exploration was easily obtained. It was quite obvious that the mass in the right flank was inflammatory tissue rising from the head of the pancreas, burrowing laterally. This pancreatic mass accounted for the filling defect seen by barium enema and the dilated cecum was partially obstructed. There were extensive areas of fat necrosis everywhere and the entire pancreas was involved. On going back over the history it became obvious that the attack of pain which he had had five weeks before entry was gallbladder disease. There was no vomiting with this attack. He had gone to Maine on a vacation and there had had a recurrence of the pain, but this time with severe vomiting which continued. The vomiting, without adequate treatment, with loss of upper intestinal contents and no fluid intake accounted for the high nonprotein nitrogen and chloride loss. With the rapid dehydration and uremia the pain of the pancreatitis disappeared into the background. I suspect that this second attack, which occurred ten days before entry was gallbladder disease complicated by acute pancreatitis. The autopsy findings corroborated what we found at operation.

CLINICAL DIAGNOSES

Preoperative: Carcinoma of the cecum with perforation.
Intestinal obstruction.
Postoperative: Chronic cholecystitis.
Cholelithiasis.
Acute pancreatitis.
Uremia.
Bronchopneumonia.
Hypertensive heart disease.

DR. EDWARD L. YOUNG'S DIAGNOSES

Intestinal obstruction?, malignancy?
Chronic cholecystitis and cholangitis.
Uremia.

ANATOMIC DIAGNOSES

Pancreatitis, acute.
Peritonitis, acute generalized.
Fat necrosis of the peritoneum.
Chronic cholecystitis.
Cholelithiasis.
Operative wound: Cholecystectomy with drainage and drainage of acute pancreatitis.
Intestinal obstruction, partial.
Hydrothorax, bilateral.
Pulmonary edema.
Diverticulum of the colon.
Arteriosclerosis, moderate, aortic.
(Hypertensive heart disease.)
Peripheral edema, marked.

PATHOLOGIC DISCUSSION

DR. MALLORY: The entire pancreas was completely necrotic and consisted of a large, swollen, hemorrhagic mass filled with areas of fat necrosis. The process had begun, as it not infrequently does in cases of pancreatitis of some days' or weeks' standing, to spread in all directions along the posterior abdominal wall so that large abscesses consisting of liquefied necrotic material were found in both gutters, running nearly the entire length of the posterior abdominal wall. The gallbladder was found at operation to contain stones, most of which were removed, though we found one still present. There were no stones in the common duct. The kidneys were a little above normal size and they showed a severe grade of chronic vascular nephritis, enough perhaps to explain his uremia, but they also showed rather marked acute degeneration of the convoluted tubules, a finding which is not uncommon in cases of pancreatitis; so that I think there was an added acute nephrosis which increased the degree of uremia beyond what it otherwise might have been.

The transverse colon appeared to be rather definitely obstructed by a mass of adhesions connecting it to the pancreas.

DR. HAMPTON: We have had three or four

cases of marked dilatation of the cecum due to inflammatory mass in the right upper quadrant, particularly the gallbladder. The patients come in with definite obstructive symptoms and the x-ray findings, particularly on a plain film, are very misleading.

CASE 22412

Presentation of Case

A sixty-four year old Danish housewife was admitted complaining of diarrhea.

Six months before entry the patient suddenly developed diarrhea, consisting of four to six loose watery movements daily. The stools were normal in color and contained neither mucus nor blood. There was no associated pain, although she frequently had a sensation of incomplete evacuation. Except for a two-day interval, during which her stools were normal in appearance and frequency, the diarrhea persisted up to admission and was unaffected by medication. The frequency was, however, slightly decreased by rest. One month prior to admission the frequency increased to ten to twenty times daily, but there was only a rare movement at night. At this time she first noted once or twice daily the passage of one or two tablespoonfuls of bright red blood. There were no tarry stools. She began to suffer occasional transient, dull, griping pain over the entire lower abdomen unrelated to meals, defecation, or activity. The pain rarely persisted for longer than a minute. She lost about eleven pounds in six months, but except for her intestinal symptoms felt quite well. There was never any nausea, emesis, fever or chills. She had lived on a farm in Massachusetts since coming to this country and had never been in the South. Her menopause occurred fourteen years previously but she had noticed the passage of foul smelling dark brown blood without clots three or four times since then. This discharge usually lasted a day or two and was never sufficiently copious to require the use of a napkin. It had last occurred one year before entry.

Twenty years previously the patient had a sudden attack of fever, rigor, profound weakness, tenesmus, and diarrhea which persisted for ten days. She had a similar attack eleven years later which lasted for about a week. There was no associated melena, nausea, or emesis.

Physical examination showed a well-developed and nourished elderly woman in no distress. There was complete edentia. The left border of cardiac dulness extended ten centimeters from the midsternal line. There was a blowing apical systolic murmur. The blood pressure was 175/120. The lungs were clear. Vaginal examination showed marked uterine procidentia. A rough mass was palpated on the posterior wall of the uterus. There was a questionable mass in the left lower quadrant. No details relative to these masses were recorded.

The temperature was 99°, the pulse 80. The respirations were 20.

Examination of an uncatheterized specimen of urine showed a specific gravity of 1.028, a slight trace of albumin, an occasional white blood cell, and 15 to 20 red blood cells. The blood showed a red cell count of 4,500,000, with a hemoglobin of 85 per cent. The white cell count was 8,300, 70 per cent polymorphonuclears. Four stool specimens were negative. Two gave positive reactions to the guaiac test, one of which contained grossly visible blood. Agglutination reactions for dysentery bacilli were negative. The serum protein was 6.2 grams per cent. A Hinton test was negative. Gastric analysis showed 0 free hydrochloric acid and 10 combined acid in a fasting specimen. After histamine the readings were 5 and 10 respectively. The blood uric acid was 5.59 milligrams per cent. An intravenous phenolsulphonephthalein test showed 35 per cent excretion of dye in two hours.

A barium enema showed the passage of barium to the midsigmoid, where a large polypoid defect was outlined. No barium passed beyond this point despite considerable ballooning of the rectum. The films showed a large irregular filling defect and several small diverticula in this region.

On the day after admission a proctoscopy showed a slightly boggy mucous membrane with a finely granular surface which bled easily. No frank ulceration was seen. There was much mucus and some pus and blood. Another proctoscopy four days later was said to have demonstrated a walnut-sized polypoid mass in the sigmoid. On the thirteenth day operation was performed.

Notes on the History

Dr. E. Parker Hayden: ". . . She frequently had a sensation of incomplete evacuation." That I suppose is synonymous with so-called tenesmus, which suggests the probability of an irritative process somewhere down near the anus.

"One month prior to admission the frequency increased to ten or twenty times daily, but there was only a rare movement at night." That point makes me wonder whether the whole thing may be on a functional rather than an organic basis, but on the other hand some decrease at night is rather to be expected because of inactivity.

"At this time she first noted once or twice daily the passage of one or two tablespoonfuls of bright red blood." In the presence of an infective or irritative process this could perfectly

well originate from low down, as the history of tenesmus and inflammation suggests that it may well have done.

The type of pain described suggests obstructive attacks. They sound like definite attacks of acute colic of some type. The duration was such that one must consider them as rather more than passing intestinal upsets.

"Vaginal examination showed marked uterine procidentia." That would perhaps explain the few episodes of dark, bloody vaginal discharge. One would expect under these circumstances that she might very well bleed from the cervix or have a vaginitis, and the blood could accumulate in the vagina while the prolapse was reduced.

"A rough mass was palpated on the posterior wall of the uterus." If the uterus was well outside, that observation is probably very reliable, because the mass must have been easy to feel, and by the same token it would seem that it probably was not in the rectum because it would be easy in a procidentia to palpate both the rectum and the uterus.

The laboratory work is essentially negative. The red cells in the catheter specimen are not to be taken seriously. We have to presume that the stools were examined while warm, with the idea of excluding amebae, although this is not mentioned.

Differential Diagnosis

The history would seem to me to suggest that there had been a definite inflammatory process of the colon dating back six months. The history of two episodes of a week and ten days of diarrhea in the past may quite well have been a factor in the situation. On the other hand one cannot be sure of that. She had lost eleven pounds in weight and yet she looked very well. We have several perfectly definite facts, the presence of a polypoid defect in the sigmoid, and a history of diverticula. In the presence of a diverticulosis with intermittent attacks of inflammation one expects episodes of looseness of the stools, but the history of six months of constant looseness, with as great frequency as she had, I do not think can be explained on the basis of diverticulitis. A benign polyp in that location ought not to produce obstruction of such degree that the roentgenologist could not force barium past it.

The fact that the proctoscopy did show a definite inflammatory process in the lower bowel, together with the history of the case, establishes the fact that she did have a colitis. It may have been rather mild at first and she may have had some bleeding without seeing it, I suppose; but the presence of true polyps in association with ulcerative colitis is quite common, and the presence of coexisting cancer also occurs with some degree of frequency. I should think that this was in all probability a case of definite inflammatory disease of the colon. It may possibly have been amebic, or it may have been an idiopathic ulcerative colitis. We know she had a polyp and it is quite possible, in fact quite probable, that she had malignant degeneration producing the obstruction in the sigmoid. On the other hand, the whole picture may have been due to diverticulitis.

Clinical Discussion

Dr. Leland S. McKittrick: I think it is a little unfortunate that on proctoscopic examination they used the statement "slightly boggy mucous membrane with a finely granular surface which bled easily" because the only way you can interpret that is as Dr. Hayden has. It is typical of a mild degree of ulcerative colitis. I happened to see this patient and, while I did not proctoscope her myself, I am sure the second proctoscopy did not show any abnormality of the mucous membrane below. I think it is fair to say that the sole finding by proctoscopy was the mass at the tip end of the instrument. Dr. Hayden has been given quite the wrong impression by the first statement in the record.

Dr. Tracy B. Mallory: I think it would be only fair to let him modify his opinion.

Dr. Hayden: We still have to explain the six months of diarrhea and this seems a little difficult to do. If she did not have definite ulceration of the mucous membrane, typical of ulcerative colitis, in the rectum, then she probably did not have ulcerative colitis. She did have a polyp. We know that she had obstruction and we know she had diverticula. She passed blood but it was bright. Her loss of weight suggests cancer, but her lack of anemia does not. The diagnosis must lie between malignant degeneration of a polyp and obstructive diverticulitis, and I incline toward the first diagnosis.

Dr. Mallory: Will you tell us what you found, Dr. McKittrick?

Dr. McKittrick: I thought she had a carcinoma of the sigmoid. I thought she had a polyp of long standing which had become malignant. I explained the past history on the basis of a benign polyp which had been present over a period of years and which ultimately became malignant. She was operated upon under that preoperative diagnosis.

At operation she had an intussusception and one could not see anything more than that at the time. It was impossible to reduce it with gentle manipulation, and whether she had a cancer or not, I did not know at the time of resection. An end-to-end anastomosis, using the Kerr technic, and a cecostomy were done. The liver was negative. There was no evidence of pelvic metastases. The pelvis was not ex-

posed, only in so far as we could see a little of it in the walling off and so forth.

PREOPERATIVE DIAGNOSES

Carcinoma of the sigmoid with obstruction.
Polyp of the sigmoid.

DR. E. PARKER HAYDEN'S DIAGNOSES

Carcinoma developing in a benign adenoma.
Diverticulosis.

PATHOLOGIC DIAGNOSES

Adenosarcoma of the sigmoid.
? Endometrioma of the sigmoid with sarcomatous degeneration.
Intussusception of the sigmoid.
Necrosis of the mucosa of the sigmoid.

PATHOLOGIC DISCUSSION

DR. MALLORY: The intussusception in this case was irreducible. When we opened the intestine we found a very unusual appearance. A polypoid tumor appeared to be projecting into the lumen. The mucosa over the tip of this was necrotic and ulcerated but there was nothing to suggest any carcinomatous change, and over the rest of the tumor it appeared fairly normal and was pouring out large amounts of mucus. Grossly the lesion was soft, not indurated.

When we made microscopic sections we found a tumor that was unlike anything I have ever seen. The mucosa except for the one necrotic area was perfectly normal. In the submucosa we found a tumor in which were various small glandular spaces lined with low columnar epithelium and a very abundant amount of actively growing fibrous stroma producing no collagen at all. It could be described as an adenosarcoma, although that seems to me only a descriptive term which really means nothing. The appearance was quite suggestive of an endometrial invasion of the wall of the sigmoid. Of course the patient's age makes that seem extremely improbable. The nearest to a reasonable guess I can make on the case is that she did have a long time in the past an adenomyoma which invaded the wall of the sigmoid as we have seen them do several times. The tumor was fairly small and caused no symptoms but within the last few months a sarcomatous degeneration of the stroma had taken place and I think that we are now dealing with a fibrosarcoma. Otherwise, I have no explanation whatever for the presence of small glands deep in the wall of the bowel, in the middle of the tumor mass, when we can completely rule out cancer. Invasive epithelial growth has certainly not taken place from the mucous membrane downward and the best guess is that it must have come in from outside.

The New England
Journal of Medicine

SUCCESSOR TO
THE BOSTON MEDICAL AND SURGICAL JOURNAL

Established in 1828

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SUBSCRIPTION TERMS: *$6.00 per year in advance, postage paid for the United States, Canada $7.04 per year, $8.52 per year for all foreign countries belonging to the Postal Union.*

Material for early publication should be received not later than noon on Saturday. Orders for reprints must be sent to the Journal office, 8 Fenway.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to The New England Journal of Medicine, 8 Fenway, Boston, Mass.

CANCER INCIDENCE HAS PASSED A PEAK

RECENTLY another gloomy report on cancer was released to the press by the famous statistician, Dr. Frederick L. Hoffman,[1] who showed that the *crude* cancer death rate in the United States is still increasing. Since then Dr. Henry D. Chadwick[2] of the Massachusetts Department of Public Health has stated that cancer is decreasing in Massachusetts. Now Dr. Louis I. Dublin[3] of the Metropolitan Life Insurance Company finds that a study of cancer among the policyholders of that company shows that deaths from cancer are *not* increasing when certain statistical factors are properly evaluated.

How is it possible that such eminent statisticians can make such totally opposing statements? It is because, as is usual in any field of knowledge where eminent men disagree, they are not talking about the same thing although they seem to be doing so.

What is the true situation in regard to cancer mortality? Whose opinion is correct? What the individual without cancer is interested in is how likely he is to develop cancer at some subsequent date and, if it appears, what his outlook for cure will be. No statistician or physician can tell anything about either of these likelihoods with any degree of accuracy as there are at present *no figures dealing directly with either problem.* All statistics on the numerical relation between cancer and population are based on deaths reported in death certificates to be due to cancer. From these figures, which by their nature are not entirely accurate to start with, statisticians have to make a sort of backhanded, indirect approach to the problem of cancer incidence.

What is the most obvious and serious source of the misleading conclusion drawn from Dr. Hoffman's statistics by those unaware of the exact meaning of his figures? There is no question that these are correct in showing that the actual number of deaths reported due to cancer are increasing, both numerically and on a basis of percentage of cancer deaths to living individuals. But this does not mean that any one individual's chance of developing cancer is increased except in so far as the possibility is greater because he will, on the average, live longer. Due to the reduction of immigration and the falling birth and death rates, the population of the United States has been aging rapidly. That this aging of the population has a very marked tendency to increase the apparent incidence of cancer deaths is clear when one considers that the number of cancer deaths per unit population at the age of 60 is roughly three times that at 50 and eight times that at 40. These enormous increases in a few years are enough to show that an average aging of the population of only one-half year would have a very significant effect on the crude cancer death rate.

Dr. Chadwick's statistics, which show a significant decrease in the Massachusetts cancer death rate, have allowed for this source of apparent error by referring each year's cancer deaths in each age group to a population of the same percentage of age distribution. This is one of the newer statistical methods which has been accepted as sound by statisticians and mathematicians and is used as a standard procedure in many parts of the world.

The enormous labor of the workers in the field of cancer is succeeding as shown by the test of results. Any individual's chance of dying from cancer is not greater but a little less than it was a few years ago, when considered on the basis of his present life expectancy.

REFERENCES

1. Hoffman, Frederick L.: The cancer record of 1935. The Spectator 137:6, 1936.
2. Chadwick, Henry D., and Lombard, Herbert L.: The Massachusetts Cancer Program. New Eng. J. Med. 215:265, 1936.
3. See page 687 of this issue of the Journal.

HARVARD MEDICAL SCHOOL IN REVIEW

THE shouting and the tumult have died away; the captains and the kings have departed and Harvard's Tercentenary Celebration lives in the memory of the exalted loyalty shown by the University's many alumni, in the rededication of our venerable institution to intellectual freedom in the search for truth, and in the more tangible, though no more valuable gifts that have been poured into her lap.

The Medical School, which has so recently celebrated its own sesquicentennial observance, played its own distinct rôle in these ceremonies and, although only half the age of its academic mother, is nevertheless old in rich traditions, though sturdy in present performance. The history of the School has been prepared for tercentenary purposes, appropriately enough, by its former dean and present Hersey Professor of the Theory and Practice of Physic, Dr. Henry A. Christian.

Founded in 1782, the Medical School of Harvard University is the second oldest in the United States, being antedated in continuous activity only by the Medical School of the University of Pennsylvania. From its inception, its faculty has played a leading rôle in the health history of the country. Its first professor of the theory and practice of physic, Benjamin Waterhouse, introduced vaccination against smallpox into America. The second professor, James Jackson, with the second professor of surgery and anatomy, John C. Warren, in 1808 prepared for the Massachusetts Medical Society the first pharmacopoeia published in the United States. These two men were largely responsible for the founding of the Massachusetts General Hospital in 1821, where, in 1846, ether anesthesia was first publicly demonstrated on a patient of the professor of surgery, John Collins Warren.

In 1831, under the leadership of Dr. Warren, Massachusetts was the first state to provide legal means by which medical students might have human bodies for dissection. Jacob Bigelow influenced medical practice with his essay on the self-limited character of disease, published in the *Boston Medical and Surgical Journal;* Henry J. Bigelow invented a method of crushing bladder stones and discovered how to reduce dislocations of the hip by manipulation; Henry I. Bowditch and Morrill Wyman first performed thoracentesis; Reginald Heber Fitz demonstrated the true nature of appendicitis and pancreatitis; Oliver Wendell Holmes fearlessly publicized the contagiousness of puerperal fever.

These are historic discoveries and advances which emanated from the Harvard Medical School. More recent progress has no less benefited from the patient studies and occasionally brilliant discoveries of a host of enthusiastic workers, animated by the desire to teach, to serve, and to follow the lines where truth might lie.

A HEALTH SURVEY

THE United States Public Health Service has been engaged in a year's study of health conditions throughout certain areas in the United States. The work has been financed by grants from the WPA and the Public Health Service. That for Massachusetts, covering a year's work, has recently been completed as far as interviewing a cross section of the people of the state and has been carried on in Boston, Pittsfield, Greenfield, Ipswich and Fall River.

Taken throughout the country seventy-nine municipalities have been included with a selection of those with a population of five thousand up to that of New York City.

Taking Boston as an example, over three thousand families have been interviewed and a similar proportion in the other municipalities.

In response to the questions asked of families, all reported illnesses during the year have been scheduled on blanks and the records thus obtained have been submitted to the attending physicians for verification of the diagnoses reported by the laity and any other pertinent facts.

The reports, after being signed by the physicians, are tabulated in the Surgeon General's office, only the nature of the illness being transferred to a card catalogue. The original report with the name of the family and the physician is destroyed, so that the disease is in the permanent record without any person's name. These filled-in family reports have been forwarded to more than a thousand physicians in Massachusetts, but the returns have not been complete. It is recognized by investigators quite generally that physicians do not return blanks submitted for the recording of factual data and for that reason much useful information is never acquired.

Already the returns have brought out material which is regarded as important by the Public Health Service, but complete returns will add a great deal to the value of this study.

We are assured that there is to be no political use of the ascertained facts and that the knowledge of conditions set forth in the completed blanks will not be used for propaganda of any kind but will be devoted to the promotion of public health service.

With this assurance and the fact that no record will be kept of the name of the physician signing a report, doctors may be willing to forward all of the reports submitted to them. Emphasis has been made on the necessity of returning a report of even one or two cases.

General co-operation by doctors will be very

much appreciated. As explained by a representative of the Public Health Service we can see no objection to sending in all of these completed blanks.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

DENNY-BROWN, DEREK ERNEST. M.B., Ch.B., University of Otago, New Zealand 1924. D. Phil., Oxford 1928. M.R.C.P., London 1931. Beit. Memor. Fellow, Oxford 1925-1928. Registrar and Resident Medical Officer, National Hospital, Queen Square 1928-1935. Assistant Physician 1935- and Chief Assistant, Neurological Clinic, St. Bartholomew's Hospital, London, 1935-. His subject is Nervous Disturbances of the Vesical Sphincter. Page 647. Address: 74 Wimpole Street, W.1, London, England.

HEPBURN, THOMAS N. A.B., A.M., M.D. Johns Hopkins University School of Medicine 1905. F.A.C.S. Urological Surgeon, Hartford Hospital. Consulting Urological Surgeon, New Britain General Hospital, New Britain; Rockville General Hospital, Rockville; Charlotte Hungerford Hospital, Torrington; Manchester General Hospital, Manchester; Meriden General Hospital, Meriden, and Bristol Hospital, Bristol. His subject is A Case of "Auto-Prostatectomy" Due to Tuberculosis. Page 653. Address: 179 Allyn Street, Hartford, Conn.

NEUSWANGER, C. H. A.B., M.S., M.D. Harvard University Medical School 1923. F.A.C.S. Assistant Clinical Professor of Surgery, Yale University School of Medicine. Assistant Attending Surgeon, New Haven Hospital. Attending Urologist, St. Mary's Hospital and Waterbury Hospital, Waterbury, Conn. His subject is Uretero-Ureteral Anastomosis with Report of a Case. Page 653. Address: 89 North Main Street, Waterbury, Conn.

PRATHER, GEORGE C. M.D. Harvard University Medical School 1924. F.A.C.S. Formerly, Assistant Urologist, Massachusetts General Hospital. Now, Assistant Urologist, Beth Israel Hospital and Boston Lying-in Hospital. Urologist, Newton Hospital. Consultant Urologist, Heywood Memorial Hospital, Norwood, Mass.; Community Hospital, Ayer, Mass., and Marlboro Hospital, Marlboro, Mass. Assistant in Anatomy, Harvard University Medical School. Address: 99 Commonwealth Avenue, Boston, Mass. Associated with him is

FRIEDMAN, HARRY F. M.D. Vanderbilt University School of Medicine 1912. Attending Radiologist and Director of Tumor Clinic, Beth Israel Hospital. Consultant Radiation Therapist, Massachusetts Memorial Hospitals and New England Hospital for Women and Children. Address: 270 Commonwealth Avenue, Boston, Mass. Their subject is The Immediate Effect of Preoperative Radiation in Cortical Tumors of the Kidney. Page 655.

PETERS, CLINTON N. A.B., M.D. Bowdoin Medical School 1914. F.A.C.S. Urologist, Maine General Hospital. Consulting Urologist, U. S. Marine Hospital, United States Public Health Service, Portland, Me. His subject is Bladder Diverticula with Reimplantation of the Ureter. Page 663. Address: 156 Free Street, Portland, Me.

THOMPSON, JUANITA. B.Sc., M.D. University of Toronto Faculty of Medicine 1928. Fellow in Bacteriology, Department of Bacteriology, University of Toronto 1928-1929. Pathologist, The Memorial Hospital, Worcester, Mass. 1929-1931. Research Associate, Department of Medical Research, Banting Institute, University of Toronto 1931-1934. Rockefeller Foundation Fellow in Neurology, Department of Neurology, New York University College of Medicine 1934-1936. Her subject is Virus Problems in Diseases of the Nervous System. Page 664. Address: 104 Mt. Auburn Street, Watertown, Mass.

THOMPSON, WILLIAM PAUL. B.S., M.D. Harvard University Medical School 1931. Research Fellow in Medicine, Harvard University Medical School. Address: 516 Park Drive, Boston, Mass. Associated with him is

LEVINE, SAMUEL A. A.B., M.D. Harvard University Medical School 1914. Assistant Professor of Medicine, Harvard University Medical School. Senior Associate Physician, Peter Bent Brigham Hospital. Address: 270 Commonwealth Avenue, Boston, Mass. Their subject is A Comparison of Accuracy in the Diagnosis of Single and Multiple Valvular Disease of the Heart. Page 670.

A PLAQUE IN MEMORY OF THE LATE WILLIAM NORTON BULLARD

On Tuesday, September 15, 1936, a hand-carved wooden plaque designed by Miss Mary O. Abbott, Concord, was dedicated to the memory of the late William Norton Bullard on the ninth floor of the Medical Building at the Boston City Hospital. Many distinguished guests, including former associates of Dr. Bullard, members of the Department of Diseases of the Nervous System of the Harvard Medical School and members of the staff of the Boston City Hospital were present. Dr. Stanley Cobb, Professor of Neuropathology, spoke of the development of neurology at the Boston City Hospital where Dr. Bullard had been associated for over twenty years. Dr. James W. Manary, Superintendent of the Boston City Hospital, spoke of the growth of the hospital with particular reference to the care of patients suffering from neurological disease. Dr. Donald Munro, Chief of the Neurosurgical Service, described his recollections of Doctor Bullard and his association with Dr. Munro's father. Dr. Merrill Moore gave a résumé of the life of Dr. Bullard. This was followed by the presentation of the memorial tablet by Mrs. William Norton Bullard. Mr. Joseph P. Manning accepted the tablet for the trustees of the hospital.

The ninth floor of the Medical Building is occupied by offices, laboratories, and teaching facilities for the Department of Neurology. The space was first occupied in 1930 when the building was completed. Dr. Bullard's influence was very important in establishing a neurological service at the Boston City Hospital. His interest in the teaching of neurology was very deep, and his influence is still felt in the hospital and at the Harvard Medical School.

The inscription on the tablet reads:

This floor is devoted
to the
WILLIAM NORTON BULLARD
MEMORIAL LABORATORIES
and the offices
of the
Neurological Unit
a joint undertaking of the
BOSTON CITY HOSPITAL
and the
HARVARD MEDICAL SCHOOL
made possible by a grant
from the
GENERAL EDUCATION BOARD
of the
Rockefeller Foundation
for the investigation and
treatment of diseases of
the nervous system

WILLIAM NORTON BULLARD, M.D.

1853—1931

William Norton Bullard was born in Newport, Rhode Island, on August 23, 1853, the son of William Story Bullard and Louisa Norton Bullard (who was a sister of Professor Charles Eliot Norton of Harvard College). He received his preliminary education in Boston schools, but when he was seventeen he was prevented by an attack of typhoid fever from entering college, and spent one year in European travel.

On returning, he entered Harvard College and re-

ceived a bachelor's degree in 1875. In 1880 he graduated, a Doctor of Medicine, from the Harvard Medical School. He served the following two years as house-pupil at the Massachusetts General Hospital. After this he went again to Europe and continued his medical studies for a year, chiefly at Vienna. On his return to Boston in 1884 he began the practice of medicine, and made neurology his specialty. He was soon appointed to the staff of the Boston Dispensary and at this time did investigative work in neurological subjects, and in 1886 published a scholarly paper on the subject of chronic tea-poisoning.* He demonstrated from a study of nearly two hundred confirmed tea-drinkers that a fairly well defined symptom-complex might be induced by overindulgence in tea.

In 1886 he established his connection with the department of nervous diseases at the Boston City Hospital. For three years he was assistant, and later was physician in this department. With his associates, Dr. Morton Prince and Dr. Philip Coombs Knapp, he worked for the enlargement of the existing neurological service to a permanent department provided with beds for the care of nervous and mental cases. During the twenty years he was connected with the Boston City Hospital, this aim was steadily approached in large measure as the result of his efforts. He left the City Hospital in 1906 to devote himself entirely to his work at the Children's Hospital where he had been Neurologist since 1888. He was particularly interested in problems concerning feeble-mindedness and in epilepsy. He wrote articles based on his investigations of these diseases as well as on functional and organic neurological topics, and, several, in collaboration with Dr. H. L. Burrell, on surgery of the central nervous system.

Dr. Bullard's enthusiasm for the study of the nervous system and its ramified disorders made him active in the foundation of the Monson State Hospital for Epileptics at Palmer, Massachusetts. As chairman of the board of trustees he did much to encourage the development of this institution, which, from a small beginning, has grown to be one of the most important of its kind in the country. He further encouraged the new science of neurology by establishing at the Harvard Medical School a chair of neuropathology now known as the Bullard Professorship.

During his medical career Dr. Bullard did much of his clinical work at the Carney Hospital in South Boston. He was also a member of the national society for the study of feeble-mindedness and of the national association for the care and study of epilepsy, and during his lifetime was president of these organizations. He was a member of the American Medical Association and the Massachusetts Medical Society. He also kept in touch with the world outside medicine through his memberships in the Somerset Club, the Harvard Club, and the Tavern Club, in which he centered his social, literary and artistic interests.

*Boston M. & S. J. **114**:314 (April 8) 1886.

Dr. Bullard had been admitted to the American Neurological Association in 1888. He became its president in 1912. In that year the society held its meeting in Boston, but he was unable to preside because of a serious operation which almost cost him his life. From this time on, his health was not good and he retired from active medical practice. He had married Miss Mary R. Reynolds, the sister of Dr. Edward Reynolds, in 1900, and with her help he gathered a large collection of rare incunabula and medical books of all centuries. It was his particular plan to compile all such books as might have been used for reference at medical schools and hospitals in the fifteenth century, including dictionaries and vocabularies. With typical generosity he lent to the Boston Medical Library in 1927 one hundred volumes of incunabula, and in the following year presented to the Library his sixteenth and seventeenth century books, numbering about five hundred volumes. This collection contains valuable and important classical texts, herbals, and books on witchcraft, magic, astrology, demonology and chiromancy. Through his will his entire collection of incunabula, as well as all other medical books, classical and modern, became the property of the Library. He also left a bequest of $50,000 to be used for the purchase of books and manuscripts published prior to 1700.

In addition to his hobby of book-collecting, Dr. Bullard was greatly interested in botany which he studied during his summers in Maine and on his frequent trips to Europe.

During the last six years of his life he was afflicted with a serious heart ailment which greatly curtailed his activities. Despite illness and failing eyesight, however, he continued his interest in neurology and public affairs. At the age of 77, while on a visit to Boston from his home in Lenox, Massachusetts, he was stricken suddenly and died on April 13, 1931.

Dr. Bullard was a man of strong personal convictions. He was genial, sympathetic and helpful to those who sought his advice. By his personal counsel and by the establishment of educational facilities he encouraged young men toward the accomplishment of their ambitions. His gift to the Boston Medical Library, the chair at the Harvard Medical School in memory of his father, and the neurological laboratories at the Boston City Hospital which are named after him bear testimony to the fact that he devoted himself and his wealth to the advancement of medical science and humanitarian ideals in the form of treatment, teaching and research in the field of diseases of the nervous system.

MERRILL MOORE, M.D.

BIBLIOGRAPHY OF WILLIAM NORTON BULLARD

A typhoid epidemic at the "North End" (Boston). Boston M. & S. J. **111**:55, 1884.
A case of progressive muscular atrophy following a blow on the head. Boston M. & S. J. **113**:369-371, 1885.
Chronic tea-poisoning. Boston: Cupples, Upham & Co., 1886.
Chronic tea-poisoning. Boston M. & S. J. **114**:314-318, 1886.
The relation of tea drinking to disorders of the nervous system. Boston M. & S. J. **117**:217-221, 1887. Also: Med. Communicat. Mass. Med. Soc. **14**:69-87, 1887.
Cases of febrile delirium tremens. Boston M. & S. J. **118**:141-148, 1888.

A case of cerebral localization, with double trephining (acquired spastic hemiplegia; porencephalus). Boston M. & S. J. **118**:162-164, 1888. Also: J. A. M. A. **10**:228-230, 1888.

Observations on the steadiness of the hand and on static equilibrium. Boston M. & S. J. **119**:595-603, 1888. (With Brackett, E. G.)

Static equilibrium. Boston M. & S. J. **118**:132, 1888. (With Brackett, E. G.)

Observations on the movements of the hand and static equilibrium. Boston: Cupples & Hurd, 1889. (With Brackett, E. G.)

Surgical operations for the relief of pressure paralysis in caries of the spine. Boston M. & S. J. **121**:405-408, 1889. Also: Tr. Am. Orthop. A. **2**:38-48, 1889. (With Burrell, H. L.)

Diffuse cortical sclerosis of the brain in children. J. Nerv. & Ment. Dis. **17**:699-709, 1890.

The significance of paroxysmal running in childhood. Boston M. & S. J. **122**:268; 278; 293, 1890.

Spastic paraplegia. Tr. Am. Orthop. A. **4**:370-374, 1891.

Provision for the care of adult pauper epileptics in Massachusetts. Boston M. & S. J. **124**:25-27, 1891.

Cerebellar tumor; operation; haemorrhage from defect of occipital bone; death. Boston M. & S. J. **124**:421-426, 1891. (With Bradford, E. H.)

Spastic paraplegia; with remarks on a case reported by Dr. C. L. Scudder. Boston M. & S. J. **126**:307, 1892.

A peculiar form of nystagmus (Cheyne-Stokes nystagmus) with a case. Boston M. & S. J. **127**:301-303, 1892. (With Wentworth, A. H.)

A consideration of some of the indications for operation in head injuries. Boston M. & S. J. **132**:73-75, 1895.

A consideration of some of the indications for operation in head injuries. Med. & Surg. Rep. Boston City Hosp. **6**:60-66, 1895.

The diagnosis of pachymeningitis interna hemorrhagica. Boston M. & S. J. **133**:461-463, 1895.

Tenotomy in spastic paralysis. Med. & Surg. Rep. Child. Hosp. 327-339, 1895.

The diagnosis of pachymeningitis interna haemorrhagica. J. Nerv. & Ment. Dis. **22**:682-684, 1895.

The surgical treatment of spastic paralysis. Med. Communicat. Mass. Med. Soc. **17**:311-316, 1896. Also: Boston M. & S. J. **135**:249, 1896.

The permanent or later results of fractures of the skull. Med. & Surg. Rep. City Hosp. Boston, 338-344, 1897. Also: Boston M. & S. J. **136**:401-406, 1897.

Increase of intradural pressure in head injuries. Boston M. & S. J. **138**:271-273, 1898.

Paralysis following cerebro-spinal meningitis. Boston M. & S. J. **140**:159, 1899.

A case of syringomyelia with unusual symptoms; autopsy; microscopical examination. Am. J. M. Sc. **117**:265-275, 1899. (With Thomas, J. J.)

The etiology of feeble-mindedness. J. Psycho-Asthenics, **7**:15-19, 1902-03.

The importance of well-made and accurately reported autopsies in the determination of the etiology of weak-mindedness and idiocy. J. Psycho-Asthenics **8**:11-15, 1903-04.

Contribution to the etiology of idiocy and imbecility. Boston M. & S. J. **150**:471-476, 1904.

The value of astereognosis as a localizing symptom in cerebral affections. J. Nerv. & Ment. Dis. **31**:241-249, 1904.

Care of epileptics in private practice. Pediatrics, N. Y. **16**:148-152, 1904.

The care of epileptics in private practice. Medicine **10**:115-118, 1904.

A case of diffuse encephalitis showing the pneumococcus. Boston M. & S. J. **151**:647-651, 1904. (With Sims, F. R.)

Results in nontraumatic surgery of the brain at the Boston City Hospital. Boston M. & S. J. **153**:78, 1905.

The relation of the epileptic to the community. Boston M. & S. J. **152**:123, 1905.

The moral responsibility of the habitual criminal. New York M. J. **81**:31, 1905.

A case of diffuse gliosis of the cerebral white matter in a child. Med. & Surg. Rep., Boston City Hosp. 19-25, 1905. (With Southard, E. E.)

A case of idiocy in a child with cystic hemispheres. Med. & Surg. Rep. Boston City Hosp. 77-86, 1905.

Cystic aplasia of the cerebral hemispheres in an idiot child. J. Med. Research **19**:431-438, 1905-06. (With Southard, E. E.)

Indications for operation in head injuries. Boston M. & S. J. **154**:184, 1906.

Affections of the spinal cord in epileptics. J. A. M. A. **47**:1717-19, 1906.

Obstetric paralysis. J. Nerv. & Ment. Dis. **33**:788, 1906. Also: Am. J. M. Sc. **134**:93-106, 1907.

Diffuse gliosis of the cerebral white matter in a child. J. Nerv. & Ment. Dis. **33**:188-193, 1906. (With Southard, E. E.)

The high-grade mental defectives. Boston M. & S. J. **159**:240-242, 1908.

Achondroplasia. Boston M. & S. J. **158**:969-971, 1908. (With George, A. W.)

A case of syringal hemorrhage complicated by meningitis. J. Nerv. & Ment. Dis. **35**:37, 1908. (With Southard, E. E.)

The placing out of high-grade imbecile girls. Boston M. & S. J. **160**:776-779, 1909.

State care of high-grade imbecile girls. Proc. Nat. Confer. Char. **37**:299-303, 1910.

Mongolian idiocy. Boston M. & S. J. **164**:56, 1911.

The new era in neurology. J. Nerv. & Ment. Dis. **39**:433-439, 1912.

A case of mild anterior poliomyelitis. Boston M. & S. J. **166**:47, 1912.

The insanity of the feeble-minded. Boston M. & S. J. **167**:873, 1912.

Mental disturbances in the feeble-minded. J. Nerv. & Ment. Dis. **42**:818-823, 1915.

OBITUARIES

Boston Evening Transcript, April 13, 1931.

Arch. Neurol. & Psychiat. **26**:179-183 (July) 1931.

The Massachusetts Medical Society

FOURTH ANNUAL POSTGRADUATE MEDICAL EXTENSION COURSE

The following sessions have been arranged by the Committee for the week beginning October 12:

Barnstable

Sunday, October 18, at 4:00 p. m., at the Cape Cod Hospital, Hyannis. Subject: Arthritis: Diagnosis and Treatment. Instructor: J. S. Barr. John I. B. Vail, Chairman.

Berkshire

Thursday, October 15, at 4:30 p. m., at the House of Mercy Hospital, Pittsfield. Subject: Diabetes: *Complications* of Diabetes and Their Treatment. Coma: Insulin Reactions; Surgery (Gangrene, Carbuncle, etc.); Marriage and Pregnancy; Tuberculosis and Heart Disease. Instructor: Alexander Marble. Melvin H. Walker, Jr., Chairman.

Essex South

Tuesday, October 13, at 4:00 p. m., at the Salem Hospital, Salem. Subject: Anesthesia: (a) Drugs in Anesthesia. (b) General Care of Patient in Anesthesia. Instructor: S. C. Wiggin. Walter G. Phippen, Chairman.

Franklin

Wednesday, October 14, at 8:00 p. m., at the Franklin County Public Hospital, Greenfield. Subject: Blood Diseases: The Hemoglobin and Red Blood Cells in Relation to Disease. Instructor: C. W. Heath. Halbert G. Stetson, Chairman.

Hampden

Thursday, October 15, at 4:00 p. m., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and at 8:00 p. m., in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke. Subject: Diabetes: General Plan of Treatment in *Uncomplicated* Cases; Diet; Insulin (Regular and Protamine); Exercise. Instructor: H. F. Root. George L. Schadt and George D. Henderson, Chairmen.

Hampshire

Wednesday, October 14, at 4:15 p. m., in the Nurses' Home of the Cooley Dickinson Hospital, Northampton. Subject: Heart Disease: Treatment of Cardiovascular Emergencies. Instructor: C. L. Derick. Robert B. Brigham, Chairman.

Middlesex East

Tuesday, October 13, at 4:00 p. m., at the Melrose Hospital, Melrose. Subject: Stomach and Duodenal Ulcer: Diagnosis and Treatment. Instructor: T. V. Urmy. Joseph H. Fay, Chairman.

Norfolk

Friday, October 16, at 8:30 p. m., at the Norwood Hospital, Norwood. Subject: Acute Abdominal Emergencies. Instructor: H. B. Loder. Hugo B. C. Riemer, Chairman.

Worcester (Milford Section)

Thursday, October 15, at 8:30 p. m., in the Nurses' Home of the Milford Hospital, Milford. Subject: Acute Abdominal Emergencies. Instructor: S. J. G. Nowak. Joseph Ashkins, Sub-Chairman.

MISCELLANY

THE CANCER PROBLEM

How the people of the United States are attacking one of the country's major health problems, involving the death of 135,000 Americans annually, was portrayed before a distinguished gathering of foreign savants attending the Second International Congress of Scientific and Social Campaign Against Cancer, which convened recently in Brussels, under the patronage of the King of the Belgiums and Queen Elizabeth.

Before this distinguished body of scientists representing many countries and races, some facts were presented which at first glance seemed to stamp the cancer situation here as a particularly gloomy one. An American speaker, Dr. Louis I. Dublin, Third Vice-President and Statistician of the Metropolitan Life Insurance Company, and a leading authority on public health problems, declared that at least half a million persons in this country are afflicted with some form of cancer and that, among white residents, out of initial groups of 100 at birth, nine males and twelve females will eventually die from cancer, if present conditions continue. But, in his summary of the entire situation, Dr. Dublin made the optimistic statement that the cancer situation in the United States is far from alarming.

Dr. Dublin limited himself in the main to a discussion of cancer mortality. He based his facts largely upon the mortality experience of the insurance company, explaining that, for the past quarter of a century, the most comprehensive statistics on cancer in this country have been available from the experience of the Metropolitan's industrial policyholders. He described cancer as a major public health problem, and said that it ranks second in this country in the list of causes of death, while twenty-five years ago it was only in seventh place.

"This change in position," Dr. Dublin explained, however, "is due primarily to a decline in the death rates of the other diseases."

"The death rate from cancer in the last 25 years," Dr. Dublin said, "rose 14.4 per cent, from 75.8 per 100,000 in 1911, to 86.7 per 100,000 in 1935. It is important, however, to point out that practically all the recorded increase in cancer occurred among males; among females the mortality from cancer declined slightly during this period."

Despite its recorded mortality increases, Dr. Dublin paradoxically questioned whether cancer has shown an actual increase as a cause of death. "If one were guided only by the recorded figures for cancer, as a whole," he said, "one would be led to believe that the death rate from this disease has increased during the last twenty-five years. More careful analysis, however, is necessary, and when such analysis is made, it leads to a very different conclusion."

More cancers are recognized now than formerly, due, Dr. Dublin explained, to improved diagnostic technic. Another factor is that, owing to the aging of the population, more and more persons are surviving to the ages where the incidence of cancer is greatest. When these factors are evaluated it becomes apparent that they account for much of the increase which the crude death rate shows.

"Indeed," Dr. Dublin continued, "we may say that the cancer situation in the United States is far from alarming. A number of forms of cancer are already showing declining trends. This is particularly true of those sites which are accessible and, therefore, more readily diagnosed. Throughout the country, public and private facilities for the treatment of cases are increasing rapidly. Under the stimulus of the American Medical Association and of the more specialized societies of cancer experts, cancer education and research are being encouraged, and a large body of physicians is being trained to diagnose and treat cases more effectively. There are today about 200 cancer centers throughout the country which measure up to the standards of equipment and trained personnel established by the American College of Surgeons. One hospital in New York alone is now carrying over 12,000 patients on its active file. Other institutions with similar services are springing up in various parts of the country. It is encouraging to find that in the three years 1932 to 1934 the American College of Surgeons registered almost 25,000 living patients without recurring symptoms five or more years after treatment. These efforts will undoubtedly stimulate the movement for better control of cancer throughout the United States."—*Metropolitan Life Insurance Company Information Service.*

REPORT OF THE MEDICAL SCHOOL OBSERVANCE OF THE HARVARD TERCENTENARY

Participation by the Harvard University Medical School in the observance of the Tercentenary of the University began, officially, on July 6, 1936, when the University placed its various buildings and activities on view. The history of the Harvard Medical School was illustrated by an exhibit at Holden

Chapel in Cambridge, the original home of the School. This historical exhibit illustrated the growth and accomplishments of the Medical School since its founding in 1782. There was also a historical exhibit of the Dental School since its founding in 1867. At the Medical School buildings in Boston a number of exhibits had been arranged illustrating the work of the various departments. These consisted chiefly of the exhibit of the Warren Anatomical Museum, the Warren Collection of Incunabula and old volumes, portraits of former members of the faculty, the museum and library of the Dental School, and an exhibit by the Anatomical Department of the dissections in the Dwight Room and of a collection of memorabilia and data associated with the history of the department, particularly with the part played by Drs. Oliver Wendell Holmes and Charles Sedgwick Minot in the teaching of the department and the introduction and development of the microscope, and of microscopic anatomy and embryology. All these exhibits were maintained during the entire summer.

The Tercentenary days specifically set apart for observance by the Harvard Medical School, the Harvard Dental School, and the Harvard School of Public Health were September 14 and 15, in conjunction with the annual meetings of the Harvard Medical and Dental Alumni Associations. During the forencon of September 14, demonstrations were held at the Medical School by the departments of Bacteriology, Pathological Chemistry, Comparative Pathology, Physiology, Physical Chemistry, and Tropical Medicine; and at many of the Boston hospitals special clinics were held by members of the University teaching staff.

For the remainder of the time a series of four symposia had been arranged, which were opened on the afternoon of September 14, with a general introduction by Dr. David L. Edsall, Dean-Emeritus of the Medical School. The first symposium on Nutrition and the Deficiency Diseases, under the chairmanship of Dr. George R. Minot, consisted of a series of nine papers by Drs. Gamble, Jones, Heath, Castle, Wolbach, Blackfan, Howe, Strauss, and Joslin. It is expected that these papers, and those of the other symposia, will be published in whole or in part in subsequent issues of this *Journal*. Dr. Castle, speaking on the relationship of defective nutrition to changes in the gastrointestinal tract, emphasized that an adequate diet is essential, lest injury be done to organs which condition the raw material of the food before it enters the nutrient media of the body. Dr. Howe discussed malnutrition from the dental standpoint and Dr. Joslin spoke on protamine insulin and its advantages. Dr. Strauss discussed nerve disorders arising from defective nutrition and pointed out that these disorders, as seen not only during pregnancy and pernicious anemia but in alcoholics, are, in the latter, associated not with the specific action of alcohol but with the dietary deficiency, chiefly in vitamin B, which is often associated with habitual alcoholism.

On September 15, three symposia were carried on simultaneously throughout the day. The first on the Central and Sympathetic Nervous Systems, under the chairmanship of Dr. Walter B. Cannon, presented a series of eight papers by Drs. White, Rosenblueth, Ayer, Davis, Gibbs, Cobb, Weiss and Putnam. Dr. Davis described the interesting electrical phenomena recently observed in relation to activity of the cerebral cortex. The analogy of these types of waves to the currents generated by heart muscle and recorded by the electrocardiogram makes them of physiologic interest as well as, possibly, of clinical value.

The symposium on the Infectious Diseases was presided over by Dr. Hans Zinsser and included a dozen papers covering a wide range of conditions of infective diseases,—typhus, influenza, gonorrhea, yellow fever, pneumonia, filariasis trichinosis, and streptococcic infections. Dr. Smillie's epidemiologic studies on the virus of influenza suggested that the possibility of employing a definitely successful preventive agent against epidemic influenza may be not far distant.

Finally, in the symposium on the endocrine glands, over which Dr. J. H. Means presided, there was a series of eight papers, beginning with one by Dr. Wislocki demonstrating some new aspects of value in regard to the blood supply of the hypophysis. In the same symposium Dr. Cutler reported his clinical, surgical experience in the relation of *diabetes insipidus* to the hypophysis and the thyroid. Drs. Aub, Hastings, Albright, and Churchill presented a group of associated papers dealing with hypophyseal-parathyroid relationships, the calcium equilibrium of the body, the action of the parathyroid hormone on the skeleton, and the surgery of the parathyroids.

Following the conclusion of these symposia, was held the annual meeting of the Harvard Medical Alumni Association, which was so largely attended that the dinner of the Association, which it had been planned to hold in Vanderbilt Hall, was at short notice transferred to the Harvard Club in Boston. Following this dinner, over which Dr. Edwin A. Locke presided with gracious distinction, there were a number of addresses. President Conant spoke of past, present, and future relations between the Medical School and Harvard College and University. Dr. Roger I. Lee spoke in behalf of the Corporation and Dr. Channing Frothingham for the Overseers. Dr. Frank H. Lahey, responding for the graduates, emphasized particularly his belief that although full-time teachers are highly desirable in laboratory subjects in the Medical School, there should always be a place for the part-time clinical teacher, whose value to the University consists in and depends upon the very fact of his active and continuous clinical experience. Dr. Alan Gregg, speaking at the conclusion of the dinner, surveyed the larger fields of the relation of medicine to the community and to human progress. All who attended this series of demonstrations and meetings must

have been effectively impressed with the progress and standing of the Harvard Medical School, the loyalty of its graduates, and the favorable position of respect and importance which it holds, not only in the University but in the community as a whole.

THE CELEBRATION OF THE USE OF ETHER

The Massachusetts General Hospital has arranged a program, for October 16, to celebrate the ninetieth anniversary of the use of ether in that hospital.

An informal luncheon will be served to invited guests at 1 o'clock to be followed by a scientific program conducted by the medical and surgical staffs.

An address by Dr. Paul D. White will be delivered at 4 o'clock in the Moseley Memorial Building.

A COURSE IN PHYSICAL THERAPY

The honor of being one of only twelve institutions in the entire country to have a course for physical therapy technicians conforming to the standard adopted by the American Medical Association in 1936 has been won by Boston University's Sargent College of Physical Education, according to an announcement made recently by Dr. Daniel L. Marsh, President, and Dean Ernst Hermann.

During the last two years of the four-year curriculum, a student may major in the field of physical therapy at Sargent College, and upon graduation the student is eligible for membership in the American Physiotherapy Association. The course is given in co-operation with the Boston University School of Medicine, and clinical work is done during the senior year in the Massachusetts General, Massachusetts Memorial, and Cambridge Hospitals, the Massachusetts Industrial School for Crippled and Deformed Children, and in various doctors' offices.

Students who elect this course are those who, after having two years of foundation work in physical education, decide that their particular interest is in remedial work rather than in teaching. The value of physical therapy lies principally in the proper application of exercise, heat and massage, and is used extensively in the aftermath of many diseases or accidents which leave an individual crippled or disabled.

CORRESPONDENCE

A SUIT AGAINST A PHYSICIAN

October 2, 1936.

Managing Editor,
New England Journal of Medicine,

In reference to the article which appeared in the September 17, 1936 issue of the *Journal*, a few days ago we received a letter from our assured, the doctor involved in the case, which we desire to have published in your next issue. His letter to us is as follows:

"I am the doctor mentioned in 'A Suit Against a Physician' in the September 17, 1936 issue of *The New England Journal of Medicine*. I now know that I have been represented at all times by the attorneys for the United States Fidelity and Guaranty Company at its expense and that all further defence by them is without cost to me. At the time the article appeared I was laboring under the erroneous impression that I might at some time have to pay personally for the defence which I am receiving, and if the publication of the article based in part on my misconception has caused the United States Fidelity and Guaranty Company any harm, I am sorry.

"I also now understand that so far I am charged only with having committed criminal acts, insurance against which would be unlawful, but that if the plaintiff should later amend his declaration and prove that I had been negligent, the disclaimer sent me would no longer operate and the Company would be liable for the judgment up to the first limits of my policy.

"I am leaving the defence of my case in the hands of the attorneys for the United States Fidelity and Guaranty Company and see no reason to bring in personal counsel."

We are rather pleased that the matter has been brought to a head and we feel that the comments made by Mr. Leland Powers, Attorney for the United States Fidelity and Guaranty Company outlining the facts in the case, will provide a thorough understanding of cases such as this. As a matter of fact, this is not a new problem inasmuch as that within two years a similar case was brought to the attention of the Society on account of another company reserving its rights under similar circumstances.

We have represented the United States Fidelity and Guaranty Company for a number of years and have handled, we believe to the satisfaction of our policyholders, hundreds of claims. In our dealings with this company we have always found them to be fair and honest.

Yours very truly,
CROSBIE-MACDONALD.

79 Milk Street, Boston.

No. 30 Federal Street
Boston
September 29, 1936.

Managing Editor,
New England Journal of Medicine,

I am enclosing some comments on your editorial, "A Suit Against a Physician," which I request that you publish in the *Journal*.

Very truly yours,
LELAND POWERS,
Attorney for United States Fidelity and Guaranty Company.

The article "A Suit Against a Physician" in the issue of September 17, 1936 contains an admirable statement of the facts of a case which I am defending as counsel for the United States Fidelity and Guaranty Company, but it also shows a misunderstanding regarding the legal limitation of the right to insure physicians and the extent to which an insurance company is permitted to furnish without expense a defense in certain cases. I have found this misunderstanding so common among members of the medical profession that I welcome this opportunity to tell Massachusetts doctors just what an insurance company can and cannot do in this state.

I think that the word "malpractice" is the cause of much of the confusion which exists, because the word is commonly applied not only to negligent acts but also to criminal acts. You can't insure against liability for criminal acts. Some years ago an insurance company endorsed policies to insure for damages on account of assault, slander, libel, undue familiarity and certain other things. The counsel for the Massachusetts Insurance Commissioner wrote the company, ordering them to eliminate this sort of coverage, stating that "contracts of insurance purporting to indemnify the insured in respect to illegal or criminal acts are contrary to public policy".

The next source of misunderstanding is a failure to distinguish between the facts in a case as they will appear in evidence and what the plaintiff alleges in his declaration. From my investigation I feel certain that, in the case referred to, the facts are exactly as stated in the article, but the plaintiff's declaration says something entirely different. It charges the doctor with false, malicious and wilful conduct, i.e., criminal act, and it does not charge him with (civil) malpractice, error or mistake. Until this case is tried or the declaration amended, it stands as an accusation of crime, against which insurance is unlawful, and therefore the insurer must disclaim for any judgment which may be obtained against the doctor under the allegations of false, malicious and wilful conduct. It does not disclaim for allegations of civil malpractice, which may be made by the plaintiff at any time up to trial or even during trial, and if the plaintiff amended and proved civil malpractice we would be liable for the judgment. I cannot emphasize too strongly that the nature of the action must be found from what the plaintiff claims and not from the true facts as they will be developed at the time of trial.

Since an insurance company cannot pay damages for criminal acts, it was once suggested by a former Attorney General that it cannot furnish a free legal defense against claims for damages based on alleged criminal acts, but because a plaintiff may change the entire nature of his cause of action by amendment, the actual alleged ground of liability may not be known until the trial is completed, at which time an action commenced with allegations of crime may become an action charging only negligence, i.e., civil malpractice, which is covered by the policy and which an insurance company must defend under its policy. Former Insurance Commissioner Brown therefore ruled that the insurance companies could and should furnish a free defense until a verdict should be found against the physician based on his alleged criminal acts.

So far as I know every insurance company writing malpractice insurance in Massachusetts has always furnished in civil actions a free defense of the doctor, no matter what the allegations in the declaration, and the suggestion in the article that the doctor might have to pay personally for the defense which my office is furnishing is contrary to the well-established practice of the insurance companies and is not supported by the wording of the disclaimer letter. As attorney for the United States Fidelity and Guaranty Company I personally defended at the sole expense of the Company several doctors charged with assault and battery.

Since physicians receive in the exercise of their functions the fullest insurance protection permitted by law, and since so far as I know no insured doctor in Massachusetts has ever had to pay personally a judgment based on a finding that he committed a criminal act, in my opinion there is no reason for suggesting that the medical profession should question the extent and quality of their insurance protection and service.

LELAND POWERS.

RECENT DEATHS

SWEETSIR—FREDERICK ELLSWORTH SWEETSIR, M.D., of Merrimac, Massachusetts, died at his home, 19 Main Street, September 29, 1936.

Dr. Sweetsir was born in Saco, Maine, in 1866 and graduated from the Bowdoin Medical School in 1888. For a number of years he served on the school committee and was a vice-president of the First National Bank of Merrimac, a director of the local savings bank, a member of the Haverhill Medical Club and the staff of the Amesbury Hospital.

Dr. Sweetsir was a Fellow of the Massachusetts Medical Society and the American Medical Association, and the Bethany Lodge of Masons.

His widow and a son, Frederick, survive him.

BARNES—WILLIAM LESTER BARNES, M.D., of 1557 Massachusetts Avenue, Lexington, Massachusetts, died September 28, 1936.

Dr. Barnes was born in Providence in 1878, graduated from Harvard College in 1900 and from the Harvard Medical School in 1904. He had served the town as school physician, town physician and health officer, and chairman of the board of health.

His medical affiliations were with the Arlington Medical Club and Fellowship in the Massachusetts Medical Society and the American Medical Association. His church association was with the Baptist Church.

Besides his widow, Dr. Barnes is survived by

three sons, William L., Arthur W., and George S., all of Lexington, and a daughter, Mrs. Etta A. Wyman, of Lynn. His mother, Mrs. Caddie E. Barnes, and two sisters, Mrs. Maude Morris and Miss Alice Barnes, all of North Attleboro, also survive him.

NOTICES

ANNOUNCEMENT

SEYMOUR I. NATHANSON, M.D., announces the opening of an office at 36 Prichard Street, Fitchburg, Massachusetts.

MEDICAL CLINIC AT THE PETER BENT BRIGHAM HOSPITAL

At 3:30 p. m. on Thursday, October 15, in the Amphitheatre of the Peter Bent Brigham Hospital, Dr. Clifford L. Derick, Associate in Medicine, Harvard Medical School and Senior Associate in Medicine, Peter Bent Brigham Hospital, will give a medical clinic. To it are cordially invited practitioners and medical students.

SPECIAL SERVICE FOR PHYSICIANS AND MEDICAL STUDENTS

A Special Service for Physicians and Medical Students will be held in the Cathedral Church of St. Paul, Boston (Tremont Street, opposite the Park Street Subway), on Sunday evening, October 18, at 7:45 p. m. Dr. J. M. T. Finney of Baltimore will speak on "Religion in Medicine". Bishop Sherrill will also speak briefly.

Tickets for reserved seats may be procured through the Medical Association or by applying to Canon Trowbridge at St. Paul's Cathedral.

SPONSORING COMMITTEE:

Dr. James H. Means, Chairman
Dr. Arthur W. Allen
Dr. Alexander S. Begg
Dr. Horace Binney
Dr. C. Sidney Burwell
Dr. Richard C. Cabot
Dr. DeWitt S. Clark
Dr. Richard S. Eustis
Dr. Henry H. Faxon
Dr. Ronald M. Ferry
Dr. Frederick C. Irving
Dr. Daniel F. Jones
Dr. William Jason Mixter
Dr. John P. Monks
Dr. Hardy Phippen
Dr. Warren R. Sisson
Dr. Richard M. Smith
Dr. Augustus Thorndike, Jr.
Dr. Kenneth J. Tillotson
Dr. James Knight Wardwell
Dr. Conrad Wesselhoeft.

MASSACHUSETTS MEMORIAL HOSPITALS

There will be a luncheon meeting of the Surgical Section in the Aid Association Room, ground floor, Talbot Memorial, 82 East Concord Street, Boston, on Friday, October 9, 1936 at 12 noon.

MILO C. GREEN, *Secretary.*

NOTICES OF MEETINGS

BOSTON CITY HOSPITAL

CONFERENCE OF CLINICAL PATHOLOGY

The monthly Conference of Clinical Pathology will be held at the Boston City Hospital, Pathological Amphitheatre, Wednesday, October 14, at 12 noon.

MASSACHUSETTS MEDICAL BENEVOLENT SOCIETY

ANNUAL MEETING

The Annual Meeting will be held at the Boston Medical Library at 5:15 p. m., on Thursday, October 22.

The Council will meet at the same place at 5:00 p. m. It includes the following officers: President, Vice-President, Treasurer, Secretary and the following Trustees: Lincoln Davis, G. S. C. Badger, W. B. Robbins, Reginald Fitz, Elliott C. Cutler, Arthur W. Allen, Lloyd T. Brown, Charles C. Lund and Charles G. Mixter.

ROBERT M. GREEN, M.D., *President,*
HILBERT F. DAY, M.D., *Secretary.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital Amphitheatre (Shattuck Street Entrance), Tuesday evening, October 13, at 8:15 p. m.

PROGRAM

Presentation of Cases.

An Anthropologist in the Medical School. By T. Wingate Todd, Henry Willson Payne Professor of Anatomy, Western Reserve University School of Medicine, Cleveland.

Medical students and physicians are cordially invited to attend.

MARSHALL N. FULTON, M.D., *Secretary.*

NORFOLK DISTRICT MEDICAL SOCIETY

PROPOSED 1936-1937 MEETINGS

October 27. 8:15 p. m. St. Elizabeth's Hospital. Communications and Case Presentations by the Staff. Details of program to be announced.

November 24. 8:15 p. m. The Beth Israel Hospital. Communications and Case Presentations by the Staff. Principal subject—Cardiology. Details of program to be announced.

January 19, 1937. 8:15 p. m. The Peter Bent Brigham Hospital. Communications and Case Presentations by the Staff. Suggested title—"Abdominal Pain from the Medical and Surgical Standpoint." Details of program to be announced.

February 23, 1937. Time, place and details of program to be announced.

March 30, 1937. 8:15 p. m. New England Deaconess Hospital. A Symposium on Diabetes entitled "A Survey of the Diabetic Work of the George F. Baker Clinic in the New England Deaconess Hospital." Communications and Case Presentations by the Staff. Drs. Elliott P. Joslin, Howard F. Root, Priscilla White, Alexander Marble and Allen P. Joslin.

May, 1937. Annual Meeting. Details to be announced.

The Secretary on behalf of the Society and its Executive Committee desires to express appreciation to the Physicians, Surgeons, Hospital Executives and others who have so kindly consented to assist us in connection with the above program.

FRANK S. CRUICKSHANK, M.D., *Secretary.*
1247 Beacon Street, Brookline.

NOTE: The Censors will meet for the examination of candidates on the first Thursday of November, 1936 and May, 1937. Fee of $10.00 is payable at the time of examination. Application blanks may be obtained by writing the Secretary furnishing name, address and name of school of graduation in medicine. Application must be made at least three weeks prior to date of examination. Candidates whose applications are on file will receive proper notices.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held on Tuesday, October 20, at 12 noon, at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston. The speaker will be LeRoy A. Schall, M.D., Surgeon, Massachusetts Eye and Ear Infirmary; Assistant Laryngologist at the Robert B. Brigham, Palmer Memorial, and Collis P. Huntington Memorial Hospitals; Consultant, United States Marine Hospital, No. 2; Consultant, Tumor Clinic, Boston Dispensary. His subject will be "Upper Respiratory Infections". All physicians are cordially invited to attend.

ACADEMY OF PHYSICAL MEDICINE

The Academy of Physical Medicine will hold its Annual Meeting in Boston, Massachusetts, at the Hotel Statler on October 20, 21 and 22, 1936.

The corrected program* is educational in character and contains symposia and reports on the newer studies and clinical developments in physical medicine presented by recognized authorities in medicine and the basic sciences.

The three-day program will open with reports of the standing committees and of special surveys by Dr. William F. Roberts, Minister of Health, St. John, N. B.; Dr. Franklin P. Lowry, Newton, Mass., and Dr. William D. McFee, Boston, followed by addresses on the physics and biology of Physical Medicine by E. Leon Chaffee, Ph.D., Gordon McKay Professor of Physics and Communication Engineering, Harvard University; Dr. Byron Sprague Price of New York and Dr. Heinrich Brugsch of Tufts College.

At 12 o'clock, noon, Dr. Frank Hammond Krusen, Mayo Clinic, Rochester, Minn., will present the Presidential Address on "The Present Status of Physical Medicine."

The afternoon session will open with an address by Dr. Winfred Overholser, Commissioner, Massachusetts Department of Mental Diseases, and a paper by Dr. William Benham Snow, New York, followed by a Fever Therapy Symposium in which Drs. Frank H. Krusen, Robert E. Peck, Clifton T. Perkins, Harry Solomon, Clarence A. Neymann and Hudson Hoagland, Ph.D., Clark University, will participate. In the evening Dr. Stafford L. Warren, Strong Memorial Hospital, Rochester, N. Y., will present the Arthur H. Ring Foundation Lecture "Fundamental Principles Concerned in the Treatment of Gonococcus Infections by Artificial Fever Therapy."

On the second day a Symposium on Physical Education under the Chairmanship of Dr. R. Tait McKenzie of Philadelphia will include: Harold T. Edwards, A.A., Harvard Fatigue Laboratory; Josephine Rathbone, Ph.D., Teachers College, Columbia University; Dean Ernst Hermann, Sargent College, and Sir Robert Stanton Woods of London. Papers on orthopedic subjects will be presented by Drs. Frederic Jay Cotton and Gordon M. Morrison of Boston and Dr. Fred H. Albee of New York, Drs. Abraham Myerson, H. Houston Merritt and Isador Coriat will present subjects in neuropsychiatry. Dr. Rebekah Wright will discuss hydrotherapy technic. Clinical papers will be presented by Dr. Mary Arnold Snow, New York; Dr. Claude L. Payzant, Boston, and William J. Schatz, Allentown, Pa.

On Thursday, October 22, a Dermatological Symposium under the Chairmanship of Dr. Francis P. McCarthy will include Drs. Francis M. Thurmon, William J. Macdonald, William Boardman, Austin W. Cheever and C. Guy Lane of Boston. The Academy will be addressed by L. L. Campbell, Ph.D., Professor of Physics, Simmons College, on "The Radiation Energy of the Electromagnetic Spectrum." A motion picture by Dr. A. Rollier, Leysin, Switzerland, "Heliotherapy and the Work Cure at the International Factory Clinic at Leysin," will be shown. Papers on radiological subjects, on physical medicine in gynecology and in gastroenterology will be presented by Dr. J. Gershon-Cohen, Philadelphia, William D. McFee, Charles W. McClure and Herman A. Osgood, Boston. An Electrosurgical Symposium will be conducted by Dr. Benedict F. Boland. Drs. Lester R. Whitaker, Prodromos Papas and DeWitt G. Wilcox of Boston and William H. Schmidt of Philadelphia will participate.

An informal dinner at the Ring Sanatorium is scheduled for Tuesday evening, October 20. The Annual Academy Banquet will take place on Wednesday evening, October 21, at the Hotel Statler.

An elaborate program has been arranged for the visiting ladies.

*The program is quite different from that published on page 661, issue of September 24.